HPS Trailer Page
for
EAST

UserID: BBadio_Job_1_of_1

Printer: cm1_3e12_gbecptr

Summary

Document	Pages	Printed	Missed
WO009852585	108	108	0
Total (1)	108	108	0

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61K 35/413, 45/06

A1

(11) International Publication Number: **WO 98/52585**

(43) International Publication Date: 26 November 1998 (26.11.98)

(21) International Application Number: PCT/CA98/00494

(22) International Filing Date: 22 May 1998 (22.05.98)

(30) Priority Data:
2,206,047 23 May 1997 (23.05.97) CA

(71) Applicant *(for all designated States except US)*: IMUTEC PHARMA INC. [CA/CA]; 1285 Morningside Avenue, Scarborough, Ontario M1B 3W2 (CA).

(71)(72) Applicant and Inventor: PERCHESON, Paul [CA/CA]; 4300 Concession 7, R.R. #4, Uxbridge, Ontario L9P 1R4 (CA).

(74) Agent: MBM & CO.; P.O. Box 809, Station B, Ottawa, Ontario K1P 5P9 (CA).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: IMMUNOMODULATING, BILE-DERIVABLE COMPOSITIONS FOR THE TREATMENT OF VIRAL DISORDERS

(57) Abstract

The present invention relates to the use of a composition exhibiting antiviral properties, comprising small molecular weight components of less than 3000 daltons, and having the following properties: a) is extractable from bile of animals; b) is capable of stimulating monocytes and macrophages *in vitro* and *in vivo*; c) is capable of modulating tumor necrosis factor production; d) contains no measurable IL-1α, IL-1β, TNF, IL-6, IL-8, IL-4, GM-CSF or IFN-γ; e) shows no cytotoxicity to human peripheral blood mononuclear cells or lymphocytes; and f) is not an endotoxin. The invention also relates to the use of the antiviral composition when used in conjunction with other drugs such as antiviral compounds or immunomodulators such as interferon.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

IMMUNOMODULATING, BILE-DERIVABLE COMPOSITIONS FOR THE TREATMENT OF VIRAL DISORDERS

FIELD OF THE INVENTION

The present invention relates to immunomodulating compositions for the treatment of viral infections, pharmaceutical compositions comprising the same, and the use of such compositions in the treatment of viral infections in mammals.

BACKGROUND OF THE INVENTION

Almost all life forms are susceptible to virus infections, including humans, animals, plants, and even bacteria. Viral infections cause countless diseases and are directly responsible for enormous annual losses of domestic crops and animals. Viruses are infectious agents characterized mainly by their small size and chemical simplicity. During a part of its infectious cycle in a cell, and sometimes even outside the cell, a virus consists only of nucleic acid, either DNA or RNA, though a mature virus particle normally exists in the form of nucleic acid encased in a protein shell.

Viral infections begin either by injection of viral nucleic acid into a cell, such as a bacterial cell, or by engulfment of whole virus and uncoating of the nucleic acid, as with animal and plant viruses. Once inside the cell, the viral nucleic acid competes with the genetic material of the host for control of cell processes. The viral nucleic acid interacts with the host genetic material in different ways, dependant upon the viral type. For example, some bacterial viruses induce synthesis of an enzyme that destroys the host nucleic acid, rendering the cellular synthesis under the exclusive control of the new virus directing synthesis of new virus particles. In other situations, host material is not destroyed and viral induced functions are supplemented by those of the host nucleic acid with the resultant production of new virus particles. In other situations, all or part of the viral nucleic acid appears to be physically inserted into the host nucleic acid. In some bacterial and animal tumor viruses, the viral nucleic acid may function to some extent to produce certain specific proteins, but whole new virus particles are not produced.

In some situations the virus will damage or destroy its host (cell) and in other situations it will live in somewhat of a symbiotic relationship within its host. Viral infections can therefore be determined

by either the presence of the virus or by the results of its infection as manifested in a disease state.

When a virus infection is latent, persistent or slow, the infection can be inapparent and chronic in which a virus-host equilibrium is established. Slow and persistent viruses are intermittently or continuously present in the infected animal and may cause diseases usually of a chronic and degenerative nature, often associated with the central nervous system. There are many examples of natural viral infections of animals, plants, bacteria, and insects as well as humans, in which there are no obvious evidences of injury or illness in the host. At one end of the spectrum, there are examples such as subclinical forms of poliomyelitis, influenza, or yellow fever, no illness is manifested, although laboratory tests can easily show the virus to be present and multiplying in the host. At the other end of the spectrum, there are examples of viruses such as type 1 herpes simplex virus which persists in a latent infection for long periods, sometimes for life, and only adversely affects the individual when nonspecific factors such as fever, precipitate attacks of cold sores.

Both DNA and RNA viruses can cause cancer and are known as tumor viruses. In a small percentage of nonpermissive cells, which allow the virus to enter but not to replicate lytically, the viral chromosome either becomes integrated into the host cell genome, where it is replicated along with the host chromosomes, or forms a plasmid. Such nonpermissive invections sometimes result in a genetic change in the host cell, causing it to proliferate in an ill-controlled way and thus transforming it into its cancerous equivalent. RNA viruses use the enzyme reverse transcriptase to transcribe the infecting RNA chains of these viruses into complementary DNA molecules that integrate into the host cell genome.

The most familiar retrovirus, called human immunodeficiency virus (HIV) enters helper T lymphocytes by first binding to a functionally important plasma membrane protein called CD4. Not only does HIV kill the helper T cells that it infects, but it also tends to persist in a latent state in the chromosomes of an infected cell without producing virus until it is activated by an unknown rare event; this ability to hide greatly complicates any attempt to treat the infection with antiviral drugs. The resultant acquired immune deficiency syndrome (AIDS) develops because of specific damage to helper T-lymphocytes, which are essential to the proper functioning of the cellular immune system. This component of the immune defenses is essential in controlling infections caused by fungi, viruses, protozoa and some bacteria. It is also thought to effectively control the growth of certain tumors.

The case definition of AIDS was initially used to identify persons with this syndrome for surveillance purposes. Since the discovery of the human immunodeficiency virus, AIDS and AIDS-related illnesses have been reclassified by the Centers for Disease Control in Atlanta. This new classification places AIDS within the context of HIV illness as groups IV C-1 (opportunistic infections) and group D (tumors) disease (CDC., MMWK., 35:334-339, 1986). The most frequently observed skin lesion is Kaposi's sarcoma. This is a multifocal systemic tumor that is characterized by the rapid generation of neovascular tissue. The sites most frequently involved are the skin, mucous membranes and lymph nodes. Usually the tumor presents with single or multiple pink, red or violet lesions that may take the form of macules, papules, plaques or nodules. With progressive disease, this tumor has been found in all organs.

Measurement of the viral load, or the number of copies of a viral genome per cell in a biological sample is important for a number of reasons. In some situations, the viral load may be the only manner of determining the seriousness of the infection or disease and whether the patient is responding to therapy. In the case of viruses responsible for a disease such as AIDS, where the infection is overshadowded by symptomatic complications, determination of the viral load might be the only manner of revealing the progress of the infection.

The problem of the combating virus infections has not yet been solved. One of the unsolved problems is the relatively rapid mutation of viruses which totally or partly prevents the effect of antiviral drugs or the body's own antibodies. Therapies are continuously being developed for the prophylaxis and treatment of predominant, devastating viral infections, such as HIV.

One approach is based on the antigen-specific elements of the immune system, namely antibodies and T-cells. For example, research has been aimed at developing vaccines against foreign agents, or against certain endogenous chemical messengers, such as interleukins, to control or induce certain antibody reactions. A second approach is based on the isolation, cloning, expression and production of peptides and proteins from the nonantigen-specific parts of the immune system. For example, proteins, such as cytokines, which comprise the interleukins produced by white blood cells, and interferons, which stimulate lymphocytes and scavenger cells that digest foreign antigens, offer possibilities for therapies.

Research in the field of tumor and virus biology has provided critical insights regarding substances

which affect their pathology. Two substances which appear to play important roles in tumor and viral growth and replication are tumor necrosis factor (TNF) and interferon (IFN).

TNF was originally termed "cachectin" because of its ability to produce the wasting syndrome cachexia. It is composed of two related proteins: mature TNF (TNFα) and lymphotoxin (TNFβ), which are primarily produced by activated macrophages, monocytes and lymphocytes. Both TNFα and TNFβ are recognized by the same cell surface receptor. TNFα was originally discovered in the serum of animals injected sequentially with the bacterial vaccine bacillus Calmette-Guerin, and endotoxin (Carswell, *et al.*, P.N.A.S. USA, 72:3666, 1975). TNFα is secreted as a soluble homotrimer of 17kD protein subunits in response to endotoxin or other stimuli (Smith, *et al.*, J.B.C., 262:6951, 1987). A membrane bound precursor form of TNFα has also been described (Kriegler, *et al.*, Cell, 53:45, 1988).

The expression of the gene encoding TNFα is not limited to cells of the monocyte/macrophage family. Several human non-monocytic tumor cell lines were shown to produce TNFα. The role of the physiologically active TNF polypeptide has been studied. In particular, TNF has been shown to induce necrosis of tumors, with no effect upon the normal tissues of the living body. The amino acid sequence of TNF, as well as the base sequence of the DNA coding for TNF, have been disclosed in U.S. Patent No. 4,879,226.

The mechanism of action of TNFα appears to be derived from accumulating evidence which indicates that TNFα is a regulatory cytokine with pleiotrophic biological activities. These activities include: inhibition of lipoprotein lipase synthesis, activation of polymorphonuclear leukocytes, inhibition of cell growth or stimulation of cell growth, cytotoxic action on certain transformed cell lines, antiviral activity, stimulation of bone resorption, stimulation of collagenase and prostaglandin E2 production and immunoregulatory actions including activation of T-cells, B-cells, monocytes, thymocytes and stimulation of the cell-surface expression of major histocompatibility complex class I and class II molecules.

The mechanisms by which TNF exerts its effect is not entirely known, but it has been suggested that they are mediated by the suppression of lipoprotein lipase activity. Serum TNF levels have been directly correlated with tumor burden in sarcoma bearing experimental animals, and inversely with food intake and body weight. Elevated levels of TNF have aslo been associated with HIV-infected

persons with AIDS or AIDS related complex, but not in asymtomatic HIV-infected persons.

Because TNF has been shown to have a role in inducing necrosis of tumors, any agent that can stimulate the production or bioavailability of TNF *in vivo* has potential utility as a treatment for various tumorous conditions. Additionally, any agent that can stimulate human monocytes and macrophages to produce TNF *in vitro*, is useful as a means for providing a source of TNF for therapeutic administration, as well as for analytical and diagnostic purposes. Unfortunately, treatments with high dosages of TNF alone have been associated with such side effects as hypotension, leukocytosis, fever, chills, neurotoxicity, nausea and vomiting.

TNF therapy has therefore played an important role in the field of cancer therapy, however excessive or unregulated TNF production has been implicated in exacerbating a number of disease states. These include rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis and other arthritic conditions, sepsis, septic shock, gram negative sepsis, toxic shock syndrome, adult resipratory stress syndrome, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcoidosis, bone resorption disease, reperfusion injury, graft v. host reaction, allograft rejections, fever and myalgias due to infection, such as influenza, cachexia secondary to infection or malignancy, cachexia secondary to AIDS, keloid formation, scar tissue formation, Crohn's disease, ulcerative colitis and pyresis plus a number of autoimmune diseases such as multiple sclerosis, autoimmune diabetes and systemic lupus erythematosis.

Cytokines, specifically TNF, have been implicated in the activation of T-cell mediated HIV protein expression and/or virus replication by playing a role in maintaining T-lymphocyte activation. Therefore, extensive research has been directed towards interfering with cytokine production, notably TNF, in a HIV-infected individual. The therapeutic aim being to limit the maintenance of T-cell activation, thereby reducing the progression of HIV infectivity to previously uninfected cells, thereby resulting in a slowing or elimination of the progression of immune dysfunction caused by HIV infection. Hence there is mounting evidence supporting the use of inhibitors of cytokines, particularly TNF, (U.S. Patent Nos. 5,563,143 and 5,506,340) in the treatment of AIDS.

Numerous clinical trials have also been carried out in patients with Kaposi's sarcoma with immune modulators such as Interferonα (J.AIDS., 1:111-118; 1988). This drug has been licensed in Canada for the treatment of Kaposi's sarcoma. Interferon has been shown to have antitumor and

antiretroviral effects. Response rates to treatment with IFN are initially high (Krown, *et al.*, Recomb. Leucocyte A IFN in Kaposi's sarcoma, N.Y. Acad. Sci., **437**:431-438, 1984). However prolonged responses are not frequent, possibly because of the emergence of anti-IFN antibodies (Autavelli, *et al.*, J.I.D. **163**:882-885, 1991). Patients invariably require chemotherapy or radiotherapy to control tumor growth. Both IFN and chemotherapy have substantial toxic side effects on bone marrow resulting in the termination of therapy (Fischl, M.A., Am. J. Med., April 10, 1991).

Both TNF and IFN individually possess antiviral activity, making them potential candidates in the treatment of viral infections and tumors. However, serious side effects have been observed in the treatment with therapeutically valuable doses of TNF and IFN which have limited their clinical usefulness.

Infectious diseases, such as those caused by viruses can only succeed by avoiding or defeating the body's immune system. The immune system mounts or elicits either or both non-specific immune responses and specific immune response factors to fight such pathogens.

Non-specific immune responses are focused on cytokine production, principally by macrophages, and serve as a prelude to specific antibody responses. The inflammatory cytokines include TNF-α and mediate an acute response directed to the injury or infection sites, which is manifested by an increased blood supply. The pathogenic bacteria or viruses are engulfed by neutrophils and macrophages in an attempt to contain the infection to a small tissue space. Macrophages, therefore, play a key role in the defense against infectious diseases as follows:

(1) processing and presentation of antigens to lymphocytes so that antibody-mediated and cell-mediated immune responses can occur;

(2) secretion of cytokines central to immune response; and

(3) destruction of antibody-coated bacteria, tumor cells or host cells.

Macrophages can ingest and kill a wide variety of pathogens, such as bacteria, fungi, and protozoa (parasites). This ability is augmented when the macrophages are "activated." Secreted products of activated macrophages are more diverse than those from any other immune cell. These regulate both pro- and anti-inflammatory effects and regulate other cell types. These products include TNF-α, IL-1β, IL-6, hydrolytic enzymes, and products of oxidative metabolism Bacteria that are eliminated primarily through this cell-mediated immune process include tuberculosis and other related

mycobacterial infections, such as atypical mycobacterial infections seen in up to 50% of AIDS patients, and anthrax, a potential bacteriological warfare agent. Fungal infections are common problems in immunosuppressed patients, such as those afflicted with AIDS or organ transplant patients.

Bile, which is secreted by the liver and stored in the gall bladder, has been investigated for various purposes, including the use of bile extracts to enhance bioavailability of drugs that are readily metabolized by normal liver function (see WO 90/12583) and to inhibit leucocytosis promotion in a mammal (see Shinoda et al., Chem. Pharm. Bull., 30, 4429-4434 (1982)). However, bile has never been considered to be a source of therapeutically useful compositions with respect to neoplastic, inflammatory or infectious diseases. Interestingly, in accordance with British Patent No. 337,797, it was suggested to use the gall bladder, itself, as a potential source of anti-cancer agents, but only after the bile had been removed from the gall bladder, and the gall bladder thoroughly washed.

Bile acids have been shown to inhibit endotoxin-induced release of TNF by a direct inhibitory effect on monocytes (Greve, *et al.*, Hepatology, **10(4)**:454, 1989). Of the bile acids investigated, deoxycholic acid was the most effective, chenodeoxycholic acid was less effective and ur?deoxycholic acid was ineffective. Other workers (Keane, *et al.*, Surgery, **95**:439, 1964) have demonstrated that bile acids produce their effect by inactivating endotoxins. A further possible explanation for the clinical effects of bile salts in this indication is a reduction in the absorption of endotoxin from the gut.

SUMMARY OF THE INVENTION

It has now been discovered that bile is an important source of a composition that has antiviral activities. In particular, it has been discovered that the composition of the present invention can exert antiviral activities as demonstrated by a significant reduction in viral load of a patient infected with HIV.

The bile composition of the present invention is obtained by extraction of bile with a water-soluble or water-miscible solvent. The extract so obtained may be further processed to remove unnecessary or undesirable components therefrom.

In one aspect, the present invention relates to a composition for use as an antiviral agent comprising small molecular weight components of less than 3000 daltons, and having one or more of the

following properties:

a) is extractable from bile of animals;

b) is capable of stimulating monocytes and macrophages in vitro and in vivo;

c) is capable of modulating tumor necrosis factor production;

d) contains no measurable level of IL-1α, IL-1β, TNF, IL-6, IL-8, IL-4, GM-CSF or IFN-γ;

e) shows no cytotoxicity to human peripheral blood mononuclear cells or lymphocytes; and

f) is not an endotoxin.

In accordance with a preferred embodiment, the composition is extracted from the bile of bovines and is capable of stimulating the release of TNF.

The composition of the invention may be prepared by (a) mixing bile from an animal, preferably a bovine, with a solvent that is soluble or miscible with water, preferably an alcohol, and preferably with an equal volume of an alcohol, to produce a bile/alcohol solution; (b) separating the solution which preferably is an alcohol-soluble fraction, and isolating therefrom a solution substantially free of alcohol, as by removing most of the alcohol, such as by the use of heat; (c) removing bile pigments from the solution to obtain a clear, yellowish liquid; (d) optionally treating the clear, yellowish liquid to substantially remove any residual alcohol; (e) removing fatty organic materials, as by extracting the clear, yellowish liquid with ether and isolating the aqueous phase; and (f) optionally removing residual ether from the aqueous phase.

The invention also relates to a pharmaceutical composition comprising the antiviral composition of the invention.

The invention further relates to a method of treating a patient with a viral infection, comprising administering to said patient an effective amount of a composition of the invention. The invention still further relates to the use of a composition of the invention in the prophylaxis and treatment of diseases and conditions caused by viral infection. The invention also relates to the use of the antiviral composition when used in conjunction with other drugs such as antiviral compounds or immunomodulators such as interferon.

These and other aspects of the present invention will become evident upon reference to the following detailed description and attached drawings. In addition, reference is made herein to various

publications, which are hereby incorporated by reference in their entirety.

BRIEF DESCRIPTION OF THE DRAWINGS

Further details of the invention are described below with the help of the examples illustrated in the accompanying drawings in which:

Figure 1 is a Reverse Phase-High Performance Liquid Chromatography (RP-HPLC) profile for a concentrated composition of the invention;

Figure 2 is an RP-HPLC profile for a concentrated composition of the invention;

Figure 3 is a RP-HPLC profile for a concentrated composition of the invention;

Figure 4 is a graph showing the effect of the composition on LPS-induced release of TNF by peripheral blood mononuclear cells (PBMNs);

Figure 5 is a bar graph showing the effect of the composition on LPS-induced release of TNF by PBMNs;

Figure 6 is an SDS gel of the composition of the invention;

Figure 7 shows the conditions and times of elution of the composition of the invention on hydrophilic HPLC (a) and the elution profile for a supernatant of the composition of the invention (b);

Figure 8 shows the elution of a precipitate of the composition of the invention on hydrophilic HPLC; and

Figure 9 is a graph showing dose response of the composition of the invention in stimulating peripheral blood monocyte function.

DETAILED DESCRIPTION OF THE INVENTION

A new biologic response modifier called VIRULIZIN™ has been in development by IMUTEC Corporation, a Toronto-based biopharmaceutical company, since 1986. VIRULIZIN™ is an immunomodulator which is hypothesized to exert anti-tumour activity via activation of macrophages, with subsequent enhancement of cell-mediated immune response to tumour. It is derived from bovine bile, and formulated as a sterile injectable product. Its precise mechanism of action remains unknown.

The "VIRULIZIN-2*y*" (2-gamma) designation refers to drug that has been standardized for potency by the new TNF-release potency bioassay. Otherwise it is the same drug as used in previous preclinical and clinical testing, which was designated either "VIRULIZIN™" or "VIRULIZIN™-2-

beta". IMUTEC Corporation now only manufactures VIRULIZIN™-2*y*.

Preclinical experimental evidence to date indicates that VIRULIZIN™-2*y* activity is associated with low molecular weight fraction material derived from bovine tissue, with unique immunomodulatory properties. The cumulative results of our studies with VIRULIZIN™ have revealed following:

(1) VIRULIZIN™ does not directly stimulate lymphocytes to synthesize DNA or undergo blastogenesis and cell division. VIRULIZIN™ does not directly stimulate the development of lymphocyte-mediated cytotoxicity.

(2) VIRULIZIN™ can stimulate normal peripheral blood monocytes to express cytocidal activity in a dose-dependent manner. The activity elicited by VIRULIZIN™ is equal to or greater than the activity produced in response to more conventional macrophage activators that are currently under investigation in cancer patients including: Gamma Interferon; Granulocyte-Monocyte Colony Stimulating Factor; Monocyte Colony Stimulating Factor; and Interleukin-12.

(3) VIRULIZIN™ can stimulate both the peripheral blood monocytes and regional, tumour-associated macrophages from cancer patients to express significant cytocidal activity. This included peritoneal macrophages from women with gynaecological malignancies and alveolar macrophages from patients with lung cancer. VIRULIZIN™ has been found to stimulate macrophages from cancer patients to kill autologous and heterologous tumour cells obtained from surgical specimens of patients. Of potentially greater importance is the finding that VIRULIZIN™ can often stimulate cancer patient macrophages that are unresponsive to stimulation with conventional activators such as gamma interferon + endotoxin.

(4) The hypersecretion of prostaglandins, both by macrophages and by tumor cells from cancer patients has been shown by Dr. Braun and others to be a principal cause of the immunosuppression seen in patients with advanced malignant disease. One determinant of the biological activity of different macrophage activators in cancer patients PBMs, therefore, is the sensitivity of the activator to arachidonic acid metabolism and the secretion by the cell of prostaglandins. The development of macrophage cytocidal function in response to VIRULIZIN™ was found to be insensitive to the inhibitory effects of prostaglandins. This

is considered important therapeutically because the effectiveness of many other biological activators is limited by prostaglandins.

(5) VIRULIZIN™ can stimulate cytocidal function in macrophages obtained from cancer patients (including pancreatic cancer) who are undergoing cytotoxic therapy. Of note is the fact that VIRULIZIN™ was more effective in stimulating tumouricidal function than conventional activators such as gamma interferon plus endotoxin. Thus, VIRULIZIN™ appears to have the potential to be combined with cytotoxic cancer treatment in appropriate clinical settings.

(6) VIRULIZIN™ can also stimulate cytocidal function in macrophages obtained from patients with Kaposi's sarcoma even at very late stages of the disease. Thus, the action of VIRULIZIN™ appears to be independent of the need for collaboration with other immune cell types including helper T-lymphocytes.

(7) Preliminary studies suggest that the macrophage cytocidal function that develops in response to VIRULIZIN™ may be associated with the expression of TNF*a* by the macrophages. However, other mechanisms for cytotoxicity may also be involved and are currently the subject of ongoing investigations.

(8) Demonstrates anti-tumour activity in a mouse tumour (plasmacytoma) model.

(9) Exhibits no toxicity in animals at doses up to 125 X the human clinical trial doses with no LD^{50} yet reached in toxicity studies.

(10) Induces the phenomenon of apoptosis in some continuous cell lines.

The central hypothesis guiding these studies is that the therapeutic efficacy of a powerful biological stimulator can depend on its ability to elicit suitable modulation of the immune system, such as by activating macrophages and/or monocytes to produce certain cytokines or promote activity to seek and remove or destroy disease-causing viruses or cells negatively affected by such viral infections. Such function could be generated by direct stimulation of resident immune cells in viral microenvironments. Alternatively, this function could be generated by stimulation of circulating immune cells if those cells were then able to home on sites of viral infection and to function in that

environment.

As hereinbefore mentioned, the present invention relates to a composition for use as an antiviral agent comprising small molecular weight components of less than 3000 daltons, and having at least one of the following properties:

a) is extractable from bile of animals;

b) is capable of stimulating or activating monocytes and macrophages in vitro and in vivo;

c) is capable of modulating tumor necrosis factor production;

d) contains no measurable level of IL-1α, IL-1β, TNF, IL-6, IL-8, IL-4, GN-CSF or IFN-γ;

e) shows no cytotoxicity to human peripheral blood mononuclear cells or lymphocytes; and

f) is not an endotoxin.

The composition of the invention can modulate tumor necrosis factor (TNF) production. A preferred composition of the invention isolated from bile from bovines, promotes the release of TNF from human peripheral blood mononuclear cells and from the pre-monocyte cell line U-937 in what appears to be physiological quantities. Because TNF is known to initiate a cascade of inflammatory and antitumor cytokine effects, the preferred composition could exert its antineoplastic effect by stimulating human leukocytes to release TNF (and possibly other cytokines).

The effect of the composition on the survival of human peripheral blood mononuclear cells (PBMNs) and lymphocytes was also examined. The composition was found to be non-cytotoxic to human PBMNs and lymphocytes.

As further exemplified below, the composition of the present invention has, among others, the following characteristics:

(1) The component or components responsible for TNF-release from PBMNs eluted early from a C_{18} RP-HPLC column.

(2) The composition causes the release of interleukin-1β (IL-1β), and the component responsible for the IL-1β release elutes early from RP-HPLC, suggesting that it is likely the same substance(s) that releases TNF.

(3) The composition also causes the release of low quantities of interleukin-2 (IL-2).

(4) The composition causes the release of granulocyte macrophage colony stimulating factor (GM-CSF);

(5) The ratio of TNF to GM-CSF release is about 2:1.

(6) It is likely that the same molecule(s), i.e., component(s), in the composition are responsible for releasing TNF, IL-1β and GM-CSF. It is possible that the composition acts to stimulate the release of multiple different cytokines, or alternatively, the composition triggers the production and release of one cytokine that in turn stimulates production and release of other cytokines.

(7) Physicochemical analysis of the composition, including the precipitates and supernatants thereof, by SDS gel electrophoresis and molecular sieve HPLC indicates that the principal components are less than 2500 daltons.

(8) Further physicochemical separation by hydrophilic (polyhydroxyethyl) molecular sieve HPLC confirms the small molecular weight of the components in the composition.

(9) Amino acid analysis before and after acid hydrolysis suggest the presence of peptide bonds, indicating the presence of peptides.

As hereinbefore mentioned, the composition of the invention may be prepared by (a) mixing bile from an animal, preferably a bovine, with an equal volume of an alcohol to produce a bile/alcohol solution; (b) separating out the alcohol soluble fraction and isolating a solution substantially free of alcohol; (c) removing bile pigments from the solution to obtain a clear, yellowish liquid; (d) treating the clear, yellowish liquid to substantially remove any residual alcohol; (e) extracting the clear, yellowish liquid with ether and isolating the aqueous phase; and (f) removing residual ether from the aqueous phase.

The composition is obtained from the bile of any animal that produces bile. While the composition may possess a different activity toward a specific disease if obtained from the bile of one species as opposed to another, a generally suitable source of bile is that taken from sharks, bovines, ovines, caprines, and porcines. In most cases, it is practical to obtain the bile of slaughtered healthy food animals, such as bovines, ovines, caprines, and porcines, for use in the preparation of the composition of the invention. The bile thus collected should come directly from the gall bladders and/or hepatic organs (as appropriate to the species' anatomy and physiology) of the slaughtered animals and should be substantially clear, thereby indicating that the bile preparation substantially free of pus or blood.

In a preferred embodiment of the method, bile from bovine sources is utilized. Bovine bile is plentiful, because, in part, relatively large quantities can be extracted from each animal. Moreover, bovines are routinely slaughtered and inspected under health-related regulations, thus such animals

provide a reliable source for preparing the composition of the invention. Furthermore, humans are less likely to have an allergic reaction to material of bovine origin.

Obviously, the entire composition so obtained may not be necessary to obtain such activity. Accordingly, it is possible to further separate, fractionate, or otherwise process the product thus obtained, and still retain the desired ability to stimulate TNF production, for example, to act against the immune system disorders that underlie various diseases. Moreover, it is envisioned that it is possible to obtain synthetically a product with the same or similar ability to stimulate TNF production and act against immune system disorders. Thus, it is envisioned that the components of the product may be identified and analyzed as to their respective contributions to the desired characteristics of TNF stimulation and ability to act against immune system disorders, among other biological effects. Moreover, it is further envisioned that such identification and analysis will be used to manufacture a synthetic form of the product.

The composition may be used without further modification by simply packaging it in vials and sterilizing. The composition may also be used in a concentrated form. A preferred concentrated form is prepared as follows. Prior to step (e) the clear, yellowish liquid may optionally be concentrated to about one-eighth of the volume of the bile/alcohol solution and after step (f) the aqueous phase may be concentrated so that it is one-tenth of the volume of the bile/ethanol solution.

The bile is mixed with an equal volume of an alcohol to produce a bile/alcohol solution, which is 50% alcohol. The alcohol may be an aliphatic alcohol, preferably methanol, ethanol, or propanol, most preferably ethanol.

A solution that is substantially free of the 50% alcohol-insoluble material may be isolated by centrifuging. Preferably, the bile/alcohol mixture is centrifuged at 3000-5000 rpm, most preferably 4200 rpm, for at least 2 hours, at about 15-25°C. The alcohol contained in the bile/alcohol-soluble fraction then may be removed by taking advantage of the different volatility of alcohol and water, using conventional methods, i.e., heating the fraction to a suitable temperature, e.g., 80-85°C, for a suitable amount of time, e.g., up to about 10 hours.

Bile pigments may be removed from the solution to obtain a clear, yellowish liquid by using activated charcoal, polyamidic microgranules, or filtration. Preferably, an activated charcoal treatment is

utilized. The procedure may be repeated in order that the solution satisfies optical density and conductivity standards.

The clear, yellowish liquid is treated to remove substantially any residual alcohol, using conventional methods. Preferably the clear, yellowish liquid is filtered using a filter having about a 1.0-3.5 μm retention, most preferably a retention of 2.5 μm.

The clear, yellowish liquid is then extracted with ether and the aqueous phase is isolated. The ether used in this step is preferably dimethyl ether, ethyl ether, n-propyl ether, isopropyl ether, or n-butyl ether, most preferably ethyl ether.

Residual ether may be removed from the aqueous phase by, for example, heating the solution up to 55°C, preferably up to about 40°C for about 5-15 hours, most preferably for about 10 hours.

The composition may be used without further modification simply by packaging it in vials and sterilizing. The composition also may be used in a concentrated form. A preferred concentrated form is prepared as follows. Prior to step (e) described hereinabove, the clear, yellowish liquid optionally may be concentrated to about one eighth of the volume of the bile/alcohol solution by, for example, heating to a temperature of less than about 85°C, preferably, to about 60°-70°C. After step (f), the aqueous phase may be concentrated so that it is one tenth of the volume of the bile/ethanol solution by, for example, heating to about 80-85°C.

In a preferred method to prepare a composition of the invention, the collected bile is mixed with an equal volume of ethyl alcohol. The bile/alcohol mixture is then centrifuged at about 4200 rpm for at least 2 1/2 hours, at about 20$\pm$2°C. The supernatant liquid is decanted and checked for pH and ethanol content. Bile pigments are then removed using activated charcoal. The treated bile/ethanol solution is then monitored for optical density (O.D.) and conductivity. O.D. levels or conductivity levels outside acceptable specifications require that the bile/ethanol solution be given additional treatment to remove bile pigments, for example treatment again with activated carbon to achieve a reading within specification limits.

Following activated carbon treatment, the solution is filtered through a filter having a 2.5 μm retention, the alcohol is evaporated off by heating to less than 85°C and the solution is concentrated

to approximately one eighth of the original bile/ethanol solution volume. The concentrated solution is cooled to between about 20-25 °C. This solution is then mixed with ethyl ether and the ether phase is discarded. Preferably, relatively small volumes of ether and strong agitation are used, such as 0.1 to 1 volume, preferably 0.2 to 0.5 volume. This step may be repeated once. The aqueous phase is heated to remove residual ether by heating up to 55 °C for about 10 hours, and further reduced in volume to one tenth of the original bile/ethanol volume by heating to about 80-85 °C. This solution is then tested for appearance, biological activity, and ethanol and ether content.

The pH of the composition may be adjusted to physiological pH, i.e. 7.4-7.5, using hydrochloric acid (1%) solution and sodium hydroxide (1% solution), and a buffered solution may be obtained using dibasic and monobasic sodium phosphate salts as buffers, using conventional methods.

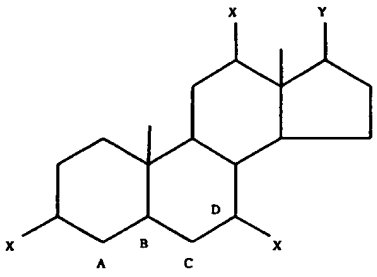
The composition may be used without further modification by simply packaging it in vials and sterilizing. A preferred sterilization method is to subject the composition to three sterilization cycles by autoclaving followed by incubation.

The composition may be used in a concentrated form. The preparation of the concentrated form is described above. The composition may also be lyophilized.

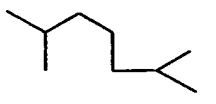
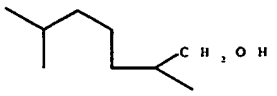
The composition and concentrated composition are clear yellowish solutions essentially free of foreign matter, containing not more than 10 ppm ethanol and not more than 5 ppm ether. The compositions activate PBMNs to release TNF in vitro as measured by the Monocyte/Macrophage Activation Assay (TNF-Release) as described in Example 2.

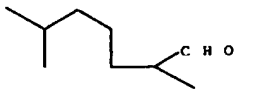
The compositions of the invention can be produced in a consistently reproducible form using the method as generally described above with demonstrated identity, potency and purity from batch to batch. Identity and purity are determined using reverse-phase high pressure liquid chromatography. (See Example 1). The compositions of the invention have a consistently reproducible pattern on reverse-phase HPLC The HPLC readings for three lots of the concentrated composition of the invention are shown in Figures 1 to 3. The compositions are also characterized by the properties hereinbefore mentioned, for example their ability to stimulate monocytes and macrophages *in vitro and in vivo*, etc.

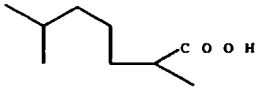
Compounds likely to be present in the present composition, considering the source, include sulfonated bile acids, oxidized bile acids, other naturally occurring bile acids, and their amino acid (especially glycine and taurine) conjugates and sterols. Accordingly, it is believed that the present composition includes at least one compound having the formula

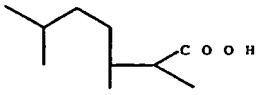


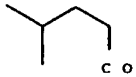
wherein the molecule may or may not be fully saturated, such that, for example, the bond between A and B, B and C, or C and D may be single or double bonds, and wherein X is H, OH, =O, or OSO_3H; and Y is

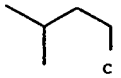

,


,


,




,


, or


; and

wherein R is an amino acid residue, such as, for example, glycyl, glutamyl, or tauryl, thereby forming the glycine, glutamyl, or taurine conjugate.

In particular, the composition of the present invention has been analyzed as to its component compounds, including organic and inorganic components. Such information was derived using standard methods of analytical chemistry, including mass spectroscopy (MS). The results of such studies include, for example, the identification of specific bile acid compounds thought to be present, including cholic acid, glycocholic acid, deoxyglycocholic acid, ursodeoxycholic acid, cholesterol

sulfate, deoxycholic acid, chenodeoxycholic acid, and taurocholic acid.

From the MS it is not distinguishable if the loss of OH and H_2 of some compounds are occurring in the MS or if the deoxy, dideoxy and unsaturated analogs of such compounds are also present to begin with. These compounds may all be present as salts of ammonium, alkylammonium and inorganic cations.

The MS analysis also supports the identification in the present composition of phospholipids, sphingolipids and related agents capable of forming miscelles. Specific compounds thought to be present include:

stearic acid $CH_3(CH_2)_{16}COOH$

palmitic acid $CH_3(CH_2)_{14}COOH$

oleic acid Z-9 octadecanoic acid $CH_3(CH_2)_2CH_2CH=CHCH_2(CH_2)_6COOH$

oxidized or hydroxylated/unsaturated short chain fatty acids: $C_6H_8O_3$

(e.g., $CH_3CH=CHCOCH_2COOH$ or a C_6 acid with 2 double bonds and a hydroxide)

acetic acid

stearic acid diglyceride

palmitic acid diglyceride

stearic acid, palmitic acid diglyceride

stearic acid-monoglyceride-phosphocholine (a lysolecithin)

stearic acid monoglyceride

stearic acid triglyceride

palmitic acid monoglyceride

phosphocholine

phosphoserine

phosphosphingosine

sphingomyelin

phosphoglycerol

glycerol

stearic acid-sphingosine

sphingosine

stearic acid amide

stearic acid methylamide

choline

glycerophosphocholine

stearic acid, oleic acid diglyceride

stearic acid, oleic acid phosphoglycerol

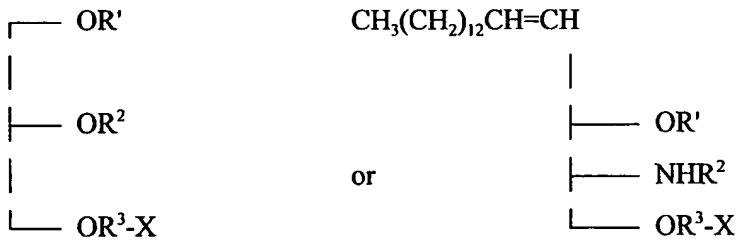
palmitic acid amide

lecithin

sialic acid-glycerol dimer

In addition, preliminary HPLC and titration evidence has been obtained which shows that shorter chain fatty acids are also present, such as those having from 1 to about 30 carbon atoms.

Phospholipid, sphingolipid, and related hydrolysis product compounds likely to be present considering the source and the information derived from the MS and HPLC analyses include at least one compound having the formula



where R', R^2, R^3 are different or the same and are H, COR^4, $CH=CH-R^5$, X, -P(O)(OH)O-, or -$S(O)_2O$-; X is selected from the group consisting of choline, ethanol amine, N-alkylated ethanolamines, serine, inositol, sugars bearing free hydroxyls, amino-sugars, sulfonated sugars, and sialic acids; R^4 is C_1-C_{30} alkyl that is saturated or unsaturated, oxidized or hydroxylated; and R^5 is an alkyl group or oxidized and/or hydroxylated analogs thereof.

The fatty acids and their conjugates may be present in the aforementioned aqueous extract as salts. The solubility of such compounds is also enhanced by other components of the mixture. Amides of the included carboxylic acids, $RCONR'R^2$, where R' and R^2 are the same or different and are H or alkyl, are also believed to be present.

A third class of compounds, namely, mucin and proteoglycan hydrolysis products, are also likely to

be present, considering the source of the composition and the aforementioned MS analysis thereof. Such compounds include hydrolysis products of mucoproteins from bile and from the gallbladder wall, such as: chondroitin 4- and 6-sulfates, dermatan sulfate, heparin, heparin sulfate, hyaluronic acid and the hydrolysis products (monomers, dimers, oligomers and polymers) of these mucins. Chitin and other mucins may be similarly hydrolyzed, which hydrolysis products would include:

N-acetyl-D-glucosamine, N-acetyl-D-galactosamine-4-sulfate, galactose-6-sulfate, N-acetyl-D-glucosamine-6-sulfate, glucosamine-6-sulfate, D-glucosamine 2-sulfate, D-glucosamine 2,3-disulfate, D-galactose-6-sulfate, glucuronic aid 2-sulfate, N-acetylneuraminic acid, sialic acid, N-acetyl chondrosine, chondroitin 4-sulfate, chondroitin 6-sulfate, D-glucosamine, D-galactosamine, glucuronic acid, glucose, galactose, mannose, fucose, iduronic acid, hexose, hexosamine, ester sulfate, glucuronic acid, chondrosamine, 2-amino-2-deoxy-D-galactose, serine, proline, threonine, alanine glycine taurine, glutamic acid, aspartic acid, histidine, and small peptides.

Similar products would be obtained by hydrolysis of mucins such as keratin sulfates, dermatan sulfates the natural sugar-sugar linkages in the dimers, oligomers and polymers may be replaced by -O-Si$(OH)_2$-O- bridges between the sugar monomers or adjacent sugar chains.

In particular, specific mucin and proteoglycan hydrolysis product compounds thought to be present include:

sialic acids and their mono and diacetylated and glycolylated monomers;
N-acetylneuraminic acid;
hexosamines, such as glucosamine;
L-fucose;
hexosamine-hexuronic acid (dimer) disulfate;
glucuronic acid;
glucuronic acid or iduronic acid disulfate, monoacetylated;
sialic acid-glycerol (dimer); and
dimers, trimers, oligomers & polymers of the above monomers in acetylated & sulfated form.

A fourth class of compounds, namely fat-soluble vitamins, likely to be present considering the source and the aforementioned MS analysis, include A, D, and K vitamins (e.g., A2, D1, D3, D4, K1, K2, K5, K6, K7, K-S(II), and Vitamin E acetate, for example.

In particular, specific fat-soluble vitamin compounds thought to be present include at least one of the group consisting of Vitamin A2, Vitamin D1, Lumisterol (present from its vitamin D1 complex), Vitamin E, Vitamin K1 oxide, and Vitamin K5.

Various miscellaneous organic compounds are likely to be present, considering the source and the aforementioned MS analysis. Such compounds include:

urea;

alkylamines, including methylamine, dimethylamine, ethylamine, methylethylamine, diethylamine, dipropylamine, and/or butylethylamine;

amino acids, including taurine, glutamic acid, glycine, alanine, n-leucine, phosphoserine, phosphoethanolamine, aspartic acid, threonine, serine, sarcosine, α-amino adipic acid, citrulline, valine, isoleucine, β-alanine, γ-amino butyric acid, hydroxylysine, ornithine, and lysine;

bilirubin, and its gluconuride conjugate;

biliverdin, and its gluconuride conjugate;

butylatedhydroxy toluene (BHT);

polyethylene glycol;

traces of steroids;

other plasma solutes, such as sugars, purines and pyrimidines;

miscellaneous dietary lipids; and

glutathione and its hydrolysis products.

In particular, specific miscellaneous organic compounds believed to be present in the composition include at least one of the group consisting of urea, methyl amine, dimethylamine, ethylamine, methylethylamine, diethylamine, dipropylamine, butylethylamine, ammonia, choline, taurine, glutamic acid, glycine, alanine, p-ser, p-eu, p-ea, asp thr ser sar, a-aba, cit, val, ile, leu, B-ala, G-aba, OH-lys, orn, lys, butylated hydroxy toluene (BHT), and polyethylene glycol.

Amines present in the present composition, particularly the secondary amines, may include

nitrogen oxides from the air, thus forming nitroso compounds. N-oxides and N-carbamate byproducts may also be included. This series of amines cited above should be extended to include all primary, secondary and tertiary alkylamines.

Certain inorganic elements have been identified and quantified (mg/l) as follows:

Tungsten	0.07
Zinc	0.666
Phosphorus	378
Cadmium	0.01
Cobalt	0.008
Nickel	0.022
Barium	0.032
Iron	0.022
Manganese	0.039
Chromium	0.060
Magnesium	7.46
Aluminum	0.136
Calcium	5.97
Copper	0.087
Titanium	0.01
Strontium	0.060
Sodium	9600
Potassium	483
Chloride	15400
Ammonia	218
Vanadium	1 ppm

The compositions of the invention may be converted using customary methods into pharmaceutical compositions. The pharmaceutical composition contain the composition of the invention either alone or together with other active substances. Such pharmaceutical compositions can be for oral, topical, rectal, parenteral, local, inhalant, or intracerebral use. They are therefore in solid or semisolid form, for example pills, tablets, creams, gelatin capsules, capsules,

suppositories, soft gelatin capsules, gels, membranes, and tubelets. For parenteral and intracerebral uses, those forms for intramuscular or subcutaneous administration can be used, or forms for infusion or intravenous or intracerebral injection can be used, and can therefore be prepared as solutions of the compositions or as powders of the active compositions to be mixed with one or more pharmaceutically acceptable excipients or diluents, suitable for the aforesaid uses and with an osmolarity that is compatible with the physiological fluids. For local use, those preparations in the form of creams or ointments for topical use or in the form of sprays may be considered; for inhalant uses, preparations in the form of sprays, for example nose sprays, may be considered. Preferably, the composition is administered intramuscularly.

The pharmaceutical compositions can be prepared by *per se* known methods for the preparation of pharmaceutically acceptable compositions which can be administered to patients, and such that an effective quantity of the active substance is combined in a mixture with a pharmaceutically acceptable vehicle. Suitable vehicles are described, for example, in Remington's Pharmaceutical Sciences (Nack Publishing Company, Easton, Pa., USA 1985).

On this basis, the pharmaceutical compositions include, albeit not exclusively, the composition of the invention in association with one or more pharmaceutically acceptable vehicles or diluents, and are contained in buffered solutions with a suitable pH and iso-osmotic with the physiological fluids.

The compositions are indicated as therapeutic agents either alone or in conjunction with other therapeutic agents or other forms of treatment. For example, other antiviral compounds, including but not limited to; 3TC, interferon, ganciclovir, famciclovir, rimantadine, foscarnet sodium, zidovudine, amantadine hydrochloride, valacyclovir, ribavirin, acyclovir, may be used in combination with the composition of the present invention. The compositions and agents of the invention are intended for administration to humans or animals.

In general, a dosage range of the composition is envisaged for administration in human medicine of from about 0.01 to 20 mg/kg, preferably from about 0.1 to l0 mg/kg, most preferably 0.1 to 1 mg/kg of body weight daily may be employed. In the case of intravenous administration, the dosage is about 0.1 to 5 mg/kg of body weight daily, and in the case of oral administration the dosage is about 1 to 5 mg/kg of body weight daily. Where the concentrated composition is used,

approximately half the above mentioned dosages may be used. For example, for intramuscular administration, a dosage of about 0.2 to 1.0 mg/kg of body weight daily, preferably 0.275-0.75 mg/kg of body weight daily may be used.

It will be appreciated by medical practitioners that it may be necessary to deviate from the amounts mentioned and, in particular, to do so as a function of the body weight and condition of the animal to be treated, the particular disease to be treated, the nature of the administration route and the therapy desired. In addition, the type of animal and its individual behavior towards the medicine or the nature of its formulation and the time or interval at which it is administered may also indicate use of amounts different from those mentioned. Thus it may suffice, in some cases, to manage with less than the above-mentioned minimum amounts while in other cases the upper limit mentioned must be exceeded. Where major amounts are administered, it may be advisable to divide these into several administrations over the course of the day.

Thus, the present invention comprises a process for preparing an antiviral composition comprising (a) mixing bile from an animal with a water-soluble solvent to produce a bile/solvent solution; (b) isolating an aqueous solution substantially free of solvent from the bile/solvent solution; and (c) removing bile pigments from the substantially solvent-free solution to obtain a clear, yellowish liquid, preferably where the water soluble solvent is an alcohol, and where the bile from the animal is mixed with an equal volume of the alcohol. Preferred aspects of the aforementioned process also comprise further concentrating the clear, yellowish liquid to about one-eighth, or one-tenth, the original volume of the bile/solvent solution. Obviously, compositions produced via the above process form a preferred aspect of the invention.

The present invention also comprises a composition for use as an immunomodulator, comprising at least one component having a molecular weight of less than about 3000 daltons, which shows no cytotoxicity to human peripheral blood mononuclear cells, and has at least one of the following properties:

(a) is capable of stimulating monocytes and macrophages *in vitro* or *in vivo* to produce one or more cytokines; and/or

(b) is capable of stimulating monocytes or macrophages to produce tumor necrosis factor *in vitro* or *in vivo*; and

wherein said component is not an endotoxin, IL-1α, IL-1β, TNF, IL-4, IL-6, IL-8, GM-

CSF or IFN-γ. Such compositions may be obtained from the bile of animals, preferably bovines, or from other sources as noted above. In a preferred embodiment of the composition, the composition stimulates tumor necrosis factor production *in vitro* or *in vivo*, and most preferably in humans, in the absence of exogenous IL-1α, IL-1β, TNF, IL-4, IL-6, IL-8, GM-CSF, and IFN-γ.

The compositions of the present invention also have components that can be characterized by column chromatography such that when said composition is dried to obtain a solid residue, and 2 grams of said residue are dissolved in 20 ml of a 10% concentrated ammonium hydroxide solution in methanol, and after any insoluble material is removed, is subjected to column chromatography in a methanol column having dimensions of 5 cm x 12.5 cm, and containing 102 g of 60 A flash silica gel, and operating at a pressure of 10 pounds per square inch and a flow rate of 11 ml/min with a 10% concentrated ammonium hydroxide in methanol solvent solution, said component is eluted from the column in a fraction taken when the total column elution is between about 180 and about 220 ml, between about 220 ml to about 260 ml, or between about 260 ml and about 300 ml.

Characterization of components may also be accomplished by ion-exchange chromatography, such that when 10 ml of said composition is subjected to anion-exchange chromatography in a column containing Bio-Rad AG-1 hydroxide form resin in an amount sufficient to bind substantially all the anions present in said 10 ml of said composition, said component is eluted from the column using a step gradient of ammonium bicarbonate buffer at a buffer concentration from about 0.1 M to about 1.5 M, preferably at a buffer concentration from about 0.2 M to about 0.4 M, and most preferably at a buffer concentration of about 0.2 M.

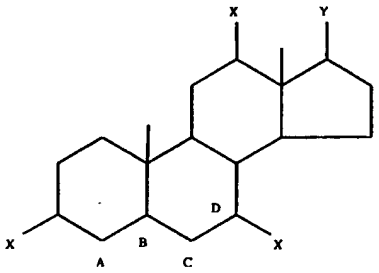
Reversed-phase (C18) HPLC can also be used for characterization of components. Other suitable columns, eluents, gradients, flow rates, operating temperatures and detection systems may be used.

The compositions of the present invention can also be characterized by TLC, such that when said composition is subjected to thin layer chromatography on silica gel plates in a suitable solvent system, such as 10% concentrated ammonium hydroxide in methanol, and visualized with a suitable spray, such as ninhydrin; a positive reaction with ninhydrin occurs at, for example, an R_f

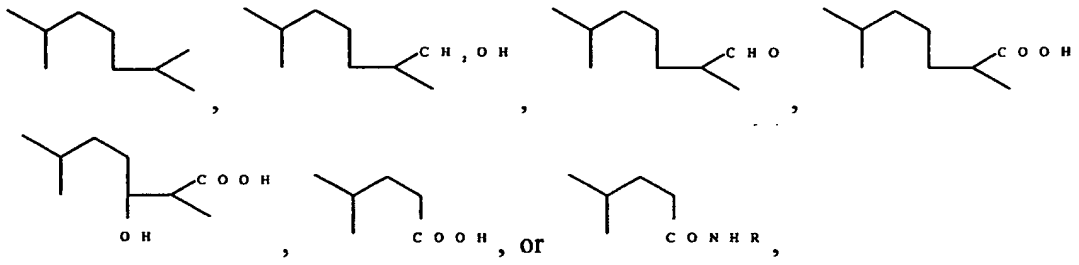
value from about 0.80 to about 0.90.

The present invention also comprises a method of stimulating tumor necrosis factor production in humans, comprising administering an effective amount of a composition comprising at least one of the following compounds:

(a) a compound of the formula



where the bonds between A-B, B-C, and C-D may be single or double bonds, and where X = H, OH, =O, or OSO_3H; and Y=



, , , , , or ,

where R is an amino acid residue;

(b) a compound of the formula

$(R^1O)CH_2CH(OR^2)CH_2(OR^3\text{-}X)$ or

$CH_3(CH_2)_{12}CH{=}CH$

|

├ OR^1

├ NHR^2

└ OR^3-X

where R^1, R^2 and R^3 are H, COR^4, CH=CH-R^5, X, P(O)(OH)O-, or -$S(O)_2O$-;

X is choline, ethanolamine, N-alkylated ethanolamines, serine, inositol, sugars bearing free hydroxyls, amino-sugars, sulfonated sugars, or sialic acids; and

R^4 is a saturated or unsaturated alkyl group having a carbon chain from about C_1 to C_{30}, or oxidized and hydroxylated analogs thereof; and

R^5 is an alkyl group or oxidized and hydroxylated analogs thereof;

(c) a mucin hydrolysis product or a proteoglycan hydrolysis product; or

(d) a fat-soluble vitamin.

Preferably, compositions of the inventive method comprise at least one compound selected from the group consisting of taurocholic acid and its sulphated derivatives; glycocholic acid and its sulphated derivatives; sphingosine; a diacyl glycerol; lecithin; phosphocholine; phosphoglycerol; glycero-phosphocholine; phosphoryl choline chloride; an oligosaccharide of less than 10 saccharide units in length, where said oligosaccharide is comprised of sialic acid, fucose, hexosamines, or sulphated hexosamines; Vitamin A; retinolic acid derivatives; retinol derivatives; taurine; and glutamic acid and its conjugates. The composition may also additionally comprise at least one compound selected from the group consisting of ammonia; primary alkyl amines; secondary alkyl amines; tertiary alkyl amines; and a carboxylic acid R^6CO_2H, wherein R^6 is C_1-C_{30} alkyl that is saturated or unsaturated, and oxidized and/or hydroxylized derivatives thereof. More preferably, such a composition comprises at least one of the group consisting of phosphocholine, glycero-phosphocholine, glucosamine-3-sulfate, and phosphorylcholine chloride. Most preferably, the composition comprises at least one of the following: phosphocholine, glycero-phosphocholine, or glucosamine-3-sulfate.

The method of the invention also embraces stimulation of TNF production by administration of a composition comprising at least one compound selected from the group consisting of taurocholic acid and its sulphated derivatives; glycocholic acid and its sulphated derivatives; sphingosine; a diacyl glycerol; lecithin; an oligosaccharide of less than 10 saccharide units in length, where said oligosaccharide is comprised of sialic acid, fucose, hexosamines, or sulphated hexosamines; Vitamin A; retinoic acid derivatives; retinol derivatives; taurine; and glutamic acid and its conjugates.

Also forming part of the present invention are compositions comprising (1) micelles of sphingosine

or sphingosine complexed with a salt, or (2) micelles of retinolic acid or its derivatives, which have at least one of the following properties:

(a) is capable of stimulating monocytes and macrophages *in vitro* to produce one or more cytokines; and/or

(b) is capable of stimulating monocytes or macrophages to produce tumor necrosis factor *in vitro* or *in vivo*.

The micelles may also comprise a diacyl glyceride or lecithin, and may further comprise a bile acid salt, and a source of ammonium or alkyl ammonium ions.

Finally, the present invention also contemplates compositions comprising (1) sphingosine, a bile acid salt and a source of ammonium or alkyl ammonium ions, (2) a bile acid salt, sphingosine, a diacyl glycerol, a source of ammonium or alkyl ammonium ions, and a retinol derivative, (3) a diacyl glyceride, lecithin, and a bile acid salt, or (4) (a) a diacyl glyceride, (b) lecithin, and (c) a mucin hydrolysis product or a proteoglycan hydrolysis product, which has at least one of the following properties:

(a) is capable of stimulating monocytes and macrophages *in vitro* to produce one or more cytokines; and/or

(b) is capable of stimulating monocytes or macrophages to produce tumor necrosis factor *in vitro* or *in vivo*.

The following non-limiting examples are illustrative of the present invention:

Example 1

This example describes and illustrates preparation of the composition of the invention.

Bovine bile was collected from the gall bladders removed from healthy cows (both males and females) that were at least one and one-half years old. These cows were slaughtered for food use at a licensed and inspected abattoir. The slaughtered animals had been inspected and evaluated as healthy prior to slaughter and the gall bladders were separated from the livers and examined by a veterinarian to confirm that the gall bladders were free of parasites and evidence of infection, and thus suitable for use as a source of bile for the present invention.

Gall bladders that passed this inspection were subjected to the following procedure: Gall bladders were wiped with a solution of 70% ethanol to sanitize the exterior of the bladders and bile was removed from the bladders with a syringe. The bile removed was visually examined in the syringe by the veterinarian to assure that it contained no blood or pus and was otherwise satisfactory. Bile from a healthy bovine is a greenish fluid substantially free of blood and pus. Fragments of livers, spleen, and lymph nodes were also collected from the animals whose bile was collected and the fragments were examined for the presence of parasites and other indications of disease.

For species that do not have a defined gall bladder (such as shark), bile is obtained directly from the hepatic organ.

Bile found to be satisfactory was transferred into a graduated amber bottle containing ethanol to give a 50% bile/50% ethanol solution by volume. The bile/ethanol solution was a greenish fluid substantially free of foreign material and tested positive for ethanol in accordance with methods recited at United States Pharmacopeia XXII, Part B (1994). These bottles were labelled with a lot number. Bile collected from a minimum of fifty animals was collected for each lot.

The bile/ethanol solution was then centrifuged at 4200 rpm for at least 2-1/2 hours at 20 ± 2° C. The supernatant liquid was decanted, filtered through a filter having, for example, a 2.5 μm retention, and checked for pH and ethanol content. The decanted liquid was then subjected to an activated charcoal treatment. The treated liquid was then monitored for Optical Density (OD) at 280 nm and conductivity. OD levels and/or conductivity levels outside specified ranges necessitated additional treatment of the liquid with activated carbon to achieve an OD and conductivity within specified ranges.

Following activated carbon treatment, the treated liquid filtered through a filter having, for example, a 2.5 μm retention, the ethanol was evaporated off (for example, by heating up to about 85° C), and the treated liquid was concentrated to approximately one-eighth of the original bile/ethanol solution volume. The concentrated liquid was then cooled to 20-25°C, filtered through a filter having, for example, a 2.5 μm retention, and mixed with ethyl ether and the ether phase was discarded. This step can be repeated once. The aqueous phase was heated to remove residual ether (for example, by heating up to about 55°C for about 10 hrs) and further reduced in volume to one-tenth of the original bile/ethanol volume by heating to around 80-85° C. The

resultant composition was then tested for appearance, biological activity, and ethanol and ether content. The composition was a clear, yellowish solution, essentially free of foreign matter, and contained less than 10 ppm ethanol and less than 5 ppm ether.

Identity and purity were determined using reverse-phase high pressure liquid chromatography (reverse-phase HPLC). Potency is assayed using the monocyte/macrophage activation test referred to herein as the peripheral blood mononuclear cell-tumor necrosis factor assay (PBMN-TNF assay or, simply, TNF assay), as described in Example 2.

Initial batches of the composition of the invention were manufactured as a non-buffered liquid. Subsequent batches were manufactured as a buffered liquid, prepared by adjusting the pH of the composition to about 7.4 ± 0.2, using hydrochloric acid (1%) solution and sodium hydroxide (1% solution), as well as using dibasic and monobasic sodium phosphate salts as buffers. Bioburden reduction was conducted in a steam autoclave at 104 ±2° C for 60 mins. The bulk solution was filled into 5 ml or 10 ml sterile bottles and capped. The filled and capped bottles were subjected to three sterilization cycles by autoclaving them at 104°C ± 2°C for 60 mins followed by incubation at 35° C for 23 ± 1 hrs. Between each cycle of sterilization (autoclave plus incubation), samples were taken and tested for bioburden. Following the last cycle of sterilization, the bottles were visually inspected against a black and a white background to detect the presence of particulates.

Following inspection, the lot was sampled and tested for conformance to specifications. Tests included identity, sterility, pyrogenicity, endotoxin, bioassay, HPLC and general safety. Table I summarizes the data obtained for the various tests performed on the bile extract of the present invention, including normal ranges of data, where appropriate.

Table I: Characteristics of Batch Compositions

Obtained In Accordance with Method of Example 1

FINAL PRODUCT TEST	BATCH # BC0248	BATCH # BC0249	BATCH # BC0250
Potency (pg/ml)*	210	183	304
Identity/Purity Agrees with reference	Pass	Pass	Pass
Safety (passes test according to 81 CFR § 610.11)	Pass	Pass	Pass

FINAL PRODUCT TEST	BATCH # BC0248	BATCH # BC0249	BATCH # BC0250
Pyrogenicity (temp. increase shall not exceed 0.4° C)	Pass	Pass	Pass
Endotoxin ≤0.4 EU/ml	≤0.25	≤0.25	≤0.25
Sterility (no growth)	Pass	Pass	Pass
pH (7.40 ± 0.2)	7.20	7.27	7.22
Appearance - Visual (clear, light yellowish liquid with little or no precipitate)	Pass	Pass	Pass
Appearance - OD (passes test)	1.34	1.38	1.85
Osmolarity (< 1000)	877	854	832
Solids (23 +/- 7mg/ml)	18	15	20
Ethanol (not more than 10 ppm)	Pass	Pass	Pass
Ethyl Ether (not more than 5 ppm)	Pass	Pass	Pass
Conductivity (35 +/- 5 mMho)	33	35	38

* Potency was measured with respect to monocyte/macrophage activation as described in Example 2; normal TNF-α release is at least 100 pg/ml.

Accordingly, the inventive composition can be prepared from readily available sources of bile, using standard laboratory methods, resulting in a standardized final product.

Example 2

This example describes the biological activity of the composition of Example 1.

Studies were conducted to evaluate the effect of the composition of Example 1 on cytokine release from peripheral blood mononuclear cells (PBMN) and/or U937 cells which is a stable line of pre-monocyte cells (American Type Culture Collection (ATCC), Rockville, Maryland). ELISA assays for TNF-α, IL-1a, IL-2, IL-4, IL-6, IL-8, GM-CSF and IFN were conducted. These studies provided the basis for a standardized test for quantitatively evaluating the potency of a given batch of bile extract prepared according to Example 1, which test evaluates the ability of the bile extract, or a component or components thereof, to stimulate TNF-α production in the PBMN or U937 cells.

Whole blood was drawn from 5 healthy human subjects into heparinized Vacutainer tubes (Beckton Dickinson, Canada). PBMNs were isolated by gradient centrifugation on Ficoll-

Hypaque (Pharmacia). The PBMNs were washed twice with phosphate-buffered saline (PBS), counted and resuspended in RPMI 1640 culture medium (Gibco Labs) at a concentration of 10^6 cells/0.5 ml. These cells were cultured in 24-well, flat-bottomed tissue culture plates (Falcon, Becton, Dickinson). A 0.5 ml aliquot of the PBMN suspension was added to each well, which contained 50 ng lipopolysaccharide (LPS) (from *E. coli*), 10 μl fetal calf serum and 10-300 μl of the composition of Example 1, as noted in the tables below. The hyperosmolar effect of the composition was neutralized by adding distilled water to the culture wells at a volume equivalent to 10% of the volume of composition used. The total volume was then made up to 1 ml/well with RPMI. PBS was used as a control. The cells were cultured for 2, 6, 24, 48 and 72 hrs at 37° C in a humidified 5% CO_2 incubator. At the end of each incubation period, the cells were harvested and cell-free culture fluids were obtained by centrifugation at 9000 rpm for 10 mins. The samples were then stored for up to 2 weeks at -70°C until immuno-assays, such as ELISA, were conducted to quantify the cytokines present.

Cytokine synthesis in the supernatants was measured after stimulating human PBMN with the composition of Example 1 at volumes of 100 and 200 μl per well. The initial preparations of the composition showed no direct (i.e., no LPS) stimulatory effect on cytokine production (see Table II). If there was any effect, it appeared that cytokine production was below the constitutive level when PBMNs were incubated in medium alone.

Table II: Direct Effect of Composition of Example 1 on Cytokine Production after 24 hrs Amount of Cytokine Released (pg/ml)[1]

		Composition		LPS
Cytokine Assayed	Medium	100 μl	200 μl	1 μg
IL-1α	61.6 ± 12	59.6 ± 7.8	54.3 ± 6.0	315 ± 117
IL-1β	199 ± 184	218 ± 165	188 ± 174	965 ± 99
TNF[2]	203 ± 149	151 ± 117	107 ± 120	1501 ± 284
IL-6	928 ± 776	853 ± 673	829 ± 543	2016 ± 41
IL-8	126 ± 70[3]	94 ± 50[3]	77 ± 41[3]	361 ± 165[3]
GM-CSF	13 ± 4	13 ± 7	15 ± 11	54 ± 20
IFN-γ	11 ± 18	9 ± 14	5 ± 6	54 ± 94
IL-4	<3.0	<3.0	<3.0	<3.0

1 Mean of eight patient samples in duplicate
2 Mean of seven patient samples in duplicate
3 ng/ml

Cytokine synthesis in the supernatants was measured at 24 hrs at 37°C after stimulating PBMNs with the composition of Example 1 and LPS (or LPS alone as positive control), using volumes of 100 μl of the composition of Example 1 per well. TNF was measured by a TNF-α ELISA kit (Endogen, Inc.), which detects a minimum level of 5 pg/ml of the cytokine. The other ELISA immunoassay kits that were used included: IL-1α (Endogen, Inc.); GM-CSF (Endogen, Inc.); RFN-α (Endogen, Inc.); IL-2 (Advanced Magnetics, Inc.); IL-6 (Advanced Magnetics, Inc.); IL-1 (Advanced Magnetics, Inc.); IL-4 (R&D Systems); and IL-8 (R&D Systems). The results indicated that TNF was the major cytokine present in the supernatants, along with smaller amounts of IL-1β and GM-CSF. For example, a 40 μl dose of the composition of Example 1 (batch B0222) stimulated the production and release of 178 pg/ml of TNF-α, 136 pg/ml GM-CSF, and 142 pg/ml of IL-1β.

Different batches of the composition of Example 1 were examined for their effect on LPS-induced release of TNF. In summary, it was found that batches of the composition produced in the same way and from the same animal induced an identical effect. However, changes in the method of preparation of the composition or use of a composition prepared from different animal species had different effects. For example, batches B29/3006, B0213, BC0241, BC0241-01, BC0242 (B = bovine) and C0203 (goat) induced a strong release of TNF above that induced by LPS alone, as shown in Table III, whereas batch 013/2109 (sheep) minimally stimulated TNF release at all doses tested. In contrast, batch R0201 (shark) inhibited TNF release at most doses tested. The TNF values shown in Table III were calculated as the difference in TNF-α release between the stimulation produced by LPS and the composition of Example 1 combined, less the stimulation produced by LPS alone.

Table III: Effect of Composition of Example 1 on LPS-Induced Release of TNF from PBMNs

Batch	Composition Volume (μl)	TNF (pg/ml)
B0213	10	193 ± 161
	100	858 ± 819
	200	2131 ± 1742
B29/3006	10	121 ±102
	50	422 ± 78

Batch	Composition Volume (μl)	TNF (pg/ml)
	100	834 ± 811
	200	2252 ± 676
C0203	10	101 ± 47
	50	643 ± 231
	100	2650 ± 1372
	200	1851 ± 980
BC0241	10	199
	25	201
	50	162
	100	339
	200	552
BC0241-01	10	170
	25	180
	50	219
	100	223
	200	589
BC0242	10	294
	25	401
	50	409
	100	603
	200	574
013/2109	50	-9 ± 73
	200	179 ± 162
Table IV	300	178 ± 373
R0201	50	145 ± 256
	200	-370 ± 385
	300	-400 ± 185

Given that the composition of Example 1 affected LPS-induced release of TNF from human PBMNs, a series of experiments were conducted to examine the effect of the composition on LPS-induced release of TNF from PBMNs over time.

Table IV: Effect of Composition of Example 1 (Batch B0213) On LPS-Induced Release Of TNF (pg/ml) from PBMNs Over Time

Time (hrs)	LPS only (50 ng/ml)	LPS + Composition (100 μl)
2	697 ± 94	693 ± 339
6	2006 ± 736	1949 ± 442
24	800 ± 222	2301 ± 658
48	170 ± 149	1419 ± 447
72	132 ± 147	945 ± 367

Table IV shows that, by 2 hours, the level of TNF release from PBMNs induced by LPS had risen to 697 pg/ml and peaked at 6 hours at about 2006 pg/ml. At 24, 48 and 72 hours, the release of TNF progressively decreased. In fact, by 48 and 72 hrs, the TNF release from LPS-induced PBMNs was just above constitutive production levels. In contrast, LPS in combination with Batch B0213 of the composition, which is a strong stimulator of TNF release, induced peak TNF release at 24 hrs, at a time when the stimulatory effect of LPS had begun to fall. Unlike LPS alone, LPS in combination with batch B0213 of the composition continued to stimulate TNF release at 48 and 72 hrs at levels well above constitute production levels. These data show that Batch B0213 of the composition of Example 1 is effective in stimulating TNF production over time.

Batch R0201 of the composition, which was derived from sharks and is an inhibitor of TNF release, markedly inhibited TNF release at 2, 6 and 24 hrs. At 48 and 72 hrs, batch R0201 had minimal positive or negative effects.

In summary, the above results indicate that some batches of the composition (e.g., from shark) inhibit TNF release from LPS-induced PBMNs, whereas other batches, such as those derived from bovine, goat, and sheep, stimulate LPS-induced TNF release. In conclusion, the composition of the invention can modulate TNF production, in both positive and negative manners. A summary of the data is shown in Figure 5 and in Table V.

Table V: Summary Of Stimulatory And Inhibitory Effects Of Compositions Of Example 1

Batch No.	Source	Normal or Concentrated	Buffer	TNF Release
B0213	Bovine	Normal	Yes	Stimulate

C0203	Caprine	Normal	Yes	Stimulate
013/2109	Ovine	Concentrated	Yes	Stimulate
R0201	Shark	Normal	Yes	Inhibit
B29/3006	Bovine	Normal	Yes	Stimulate
B27/2806	Bovine	Normal	Yes	Stimulate
B15/1606	Bovine	Concentrated	Yes	Stimulate

The PBMN-TNF assay as described above was standardized using 100 μl of the composition of Example 1 and 50 ng of LPS. PBMNs from 3 different human subjects were obtained as described above and used the same day. The results of each of the three assays (using individual subject cells) were averaged to compensate for variations in response between different subjects. The analysis involved determining the amount of TNF-α released in RPMI media alone and in the presence of 50 ng LPS. The TNF-α released in the presence of 100 μl of the composition of Example 1 in combination with 50 ng LPS was also determined. The TNF-α released in media was subtracted from the LPS value to obtain the TNF-α released in the presence of LPS alone. The media and LPS values were subtracted from the combined composition and LPS value to obtain the TNF-α released in the presence of the composition alone (reported in pg/ml). Accordingly, the TNF release assay served to quantify the potency of the bile extract.

The composition was also found to stimulate release of TNF-α from U937 cells, which were originally derived from a patient with histocytic lymphoma and display many characteristics of monocytes. U937 cells can be obtained from the ATCC. They are routinely maintained in RPMI-1640 medium (GIBCO, Grand Island, NY) supplemented with 10% heat-inactivated fetal calf serum (FCS, GIBCO), 2 mM L-glutamine (ICN Biomedical Inc, Costa Mesa, CA), and 10 μg/ml Gentamycin Sulfate (SIGMA, Mississauga, Ontario, Canada) at 37°C, 5% CO_2. Passage of the U937 cells was performed every 3-4 days and seeding was at an initial concentration of 5 x 10^5 cells/ml. The U937 cells can be stimulated to differentiate to monocytes by exposure to phorbol 12-myristate 13-acetate (PMA; Sigma Chemical Co., St. Louis, MO). The resulting monocytes have the capacity to release TNF upon stimulation, such as with the composition of Example 1, alone or in combination with LPS.

PMA was first dissolved in dimethyl sulfoxide (DMSO, SIGMA) at a concentration of 10 mM

and then diluted 1000-fold with PBS to a stock solution concentration of 10 μM and stored at -20°C. U937 cell suspensions were centrifuged at 350 x g for 10 mins at room temperature and reconstituted in fresh complete RPMI-1640 medium at a concentration of 2 x 10^6 cells/ml. Cell viability was determined by trypan blue exclusion and was routinely greater than 95%. PMA was further diluted 500-fold with complete culture media to a concentration of 20 nM.

Aliquots of 0.5 ml of U937 cells (10^6 cell/ml) were cultured in the presence or absence of 0.5 ml of PMA (20 nM) in 24-well, flat-bottom tissue culture plates (Becton Dickinson, Lincoln Park, NJ) and incubated for 72 hrs at 37°C, 5% CO_2. The final concentrations per well were 5 x 10^5 cells and 10 nM PMA.

After 72 hrs of incubation, 120 μl of media were removed and replaced by 100 μl of the composition of Example 1 and 10 μl of sterile deionized distilled water, in the presence or absence of 10 μl of LPS (5 ng/μl). After 24 hrs of incubation, any cells and particulate matter were pelleted by centrifugation at 350 x g for 10 min and the resulting supernatants were stored at -20°C until they were assayed for TNF-α. All the Virulizin samples were tested on two separate occasions.

Two-site sandwich ELISAs were performed to quantify TNF-α in the U937 cell culture supernatants using TNF-α ELISA kits purchased from Endogen, Inc. (Cedarlane Laboratories, Hornby, Ontario). The protocol recommended by the manufacturer was used. Briefly, 100 μl of TNF-α standards and test samples were added to antihuman TNF-α pre-coated 96-well plates and incubated at 37°C, 5% CO_2 for 3 hrs. After extensive washing with washing buffer, 100 μl of antihuman TNF-α conjugated to alkaline phosphatase were added to plates and incubated at 37°C, 5% CO_2 for 2 hrs. After incubation, the plates were washed as described above and 100 μl of premixed TMB substrate was added to each well and the enzymatic color reaction was allowed to develop at room temperature in the dark for 30 min. Then 100 μl of stop solution was added to each well to stop the reaction and the plates were read using an SLT Lab Instrument ELISA reader at 450 nm. The detection limit of the assay was 5 pg/ml.

TNF values for U937 cells were determined as described for PBMN cells. Results of the composition tested with 50 ng LPS are presented in Table III.

Table VI: Effect of Composition on TNF Release from U937 Cells

Composition Batch Number (100 μl)	TNF (pg/ml)
BC0241	4900
BC0241-01	4028
BC0242	6746
BC0247	5534
BC0248	6053
BC0249	5540
BC0250	5794

Example 3

This example describes the physical, chemical and biochemical characteristics of the composition of Example 1.

Physicochemical characteristics, such as conductivity, osmolarity, and total solids, for three manufactured batches of a composition prepared in accordance with Example 1 were determined. The results, tabulated in Table I, demonstrate the sterility, potency, and reproducibility of the manufactured product, and thereby provide a product specification. The ethanol and ethyl ether tests are in-process tests only. Potency, i.e., the TNF release was determined as described in Example 2. The methods used to determine the characteristics are tabulated below.

Table VII: Characteristics Of Compositions Of Example 1 As Products Of Manufacture

Test	Specification	Method
Potency	> 100 pg/ml TNF-α	Monocyte/macrophage activation: TNF-α release
Identity/Purity	Agrees with reference	HPLC
Safety	Passes test	General safety test (mice and guinea pigs) (21 C.F.R. § 610.11)
Pyrogenicity	Temperature increase shall not exceed 0.4°C	Pyrogen test (rabbits) USP
Endotoxin	< 2 EU/ml	Limulus Amoebocyte Lysate Test USP

Test	Specification	Method
Sterility	No growth	Sterility Test USP
pH	7.40 ± 0.2	pH test USP
Appearance	Clear, light yellowish liquid with little or no precipitate	Visual Inspection
Solids	23 ± 7 mg/ml	Lyophilization
Osmolarity	< 1000 mOsm	Freezing point depression USP
Ethyl Alcohol	Not more than 10 ppm	Direct Injection Gas Chromatography
Ethyl Ether	Not more than 5 ppm	Direct Injection Gas Chromatography
Conductivity	35 ± 5 mMHO	Copenhagen Radiometer Model

The above-described physical and chemical properties, such as conductivity, osmolarity and total solids, were consistent with a composition that is over 99% salt. Less than 1% of the solids in the composition was organic material, around half of the solids were carbohydrates, and the rest were amino acids, lipids, and phospholipids. Proteins and peptides were present. SDS gel electrophoresis confirmed that there were more peptides than proteins in the composition. High molecular weight molecules were not detected.

HPLC and bioassay test methods for the composition of the invention were used to characterize the product as the buffered liquid and the concentrated formula. The HPLC results described below indicate that the product was the same in all of its presentations.

A tandem column reverse-phase HPLC method was used to characterize the composition of Example 1. For this method, samples were lyophilized and then reconstituted in Buffer A (0.1% trifluoroacetic acid (TFA)) and were run on a WP60009-C18 column (W-Pore C18, 250 X 4.6 mm; Phenomenex of California) in tandem with a prime-sphere HC-C18 column (250 X 4.6 mm; Phenomenex). The columns were run at ambient temperature using Buffer A and Buffer B (0.1% TFA in 100% acetonitrile), with a flow rate of 0.9 ml/min. A 150 µl sample was applied to the first column and Buffer A was run through the system for 20 mins. Next, a first linear gradient, 0-80% Buffer B, was run over 35 mins, followed by a second linear gradient, 80-0% Buffer B, over 5 mins. Eluted compounds were detected via optical absorbance at from 190 to 284 nm, with most

runs being detected at 210 and 235.

The composition of Example 1 had a consistently reproducible pattern on reverse-phase HPLC in which peaks were seen. The reverse-phase HPLC readings for three lots of the composition of the invention are shown in Figures 1-3.

Six batches of bile extract, which were prepared as in Example 1 and labeled A-F, were analyzed for their amino acid profiles on an LKB 4151 Alphaplus amino acid analyzer operated in a physiological mode, with post-column detection with ninhydrin. The results, in nmoles/100 µl, are shown in Table VIII.

Table VIII : Amino Acids And Urea Profiles Of Compositions Of Example 1

Amino Acids and Urea	A	B	C	D	E	F
P-Ser	0.342	0.429	0.473	3.239	1.454	1.048
Tau	3.438	8.325	2.515	11.297	23.005	47.019
Urea	23.318	35.224	146.806	608.984	98.489	115.26
Asp	0.606	1.060	1.163	-	-	-
Thr	0.649	0.483	-	0.345	12.646	1.548
Ser	1.104	0.833	0.452	0.821	-	-
Glu	2.112	8.257	8.029	13.333	36.169	43.632
Gly	5.465	15.667	6.341	12.625	38.842	82.418
Ala	2.634	4.449	3.572	6.093	32.662	23.202
Val	0.942	0.645	0.550	1.311	15.521	4.362
Ile	-	-	-	-	3.089	-
Leu	-	-	0.186	1.079	7.300	1.197
B-Ala	0.387	0.503	0.450	1.060	1.461	2.640
Orn	-	-	-	0.102	0.412	0.336

Samples A-F were also assessed for presence of bovine DNA. The samples were examined utilizing a ^{32}P-labeled bovine DNA probe generated from bovine genomic DNA. The assay included the samples, spiked samples, negative and positive controls, and standards. The study was conducted in compliance with GLP regulations. This assay detected 3.9 pg of reference standard DNA. Each of the samples was calculated to contain less than 4 pg/ml DNA.

Samples A-F were also tested for the presence of various electrolytes. This analysis was provided by the Biotechnology Service Centre, Department of Clinical Biochemistry, University of Toronto. The results, in mmole/l, are shown in Table IX.

Table IX: Electrolyte Content of Compositions of Example 1

Electrolyte	A	B	C	D	E	F
NA	55	68	127	359	250	309
K	0.9	0.9	2.5	10.2	3.6	4.2
Ca	0.06	0.10	0.006	0.2	0.13	0.27
Mg	0.25	0.15	0.09	0.35	0.14	0.17
Cl	50	59	118	386	207	263
PO_4	0.06	0.03	0.05	0.27	0.18	0.24
SO_4	2.17	1.89	2.05	1.15	7.13	11.36

Samples A-F were submitted to semi-quantitative multi-element analysis by inductively coupled mass spectrometry (ICP-MS) under standard conditions. The results, in parts per million (ppm), are described in Table X.

Table X: Elemental Analysis of Compositions of Example 1

	A	B	C	D	E	F
Scandium	0.620	0.820	1.030	1.030	2.020	1.900
Titanium	0.210	0.310	0.260	0.720	0.920	1.180
Vanadium	0.030	0.040	0.080	0.180	0.140	0.160
Chromium	0.030	0.040	0.060	0.080	0.170	0.190
Iron	0.300	0.380	0.510	4.310	0.690	0.760
Manganese	0.020	0.020	0.030	0.530	0.050	0.060
Nickel	<det	<det	0.030	0.250	0.130	0.160
Cobalt	<det	<det	0.001	0.013	0.003	0.005
Copper	0.700	0.940	0.840	1.520	2.140	2.470
Zinc	15.600	18.300	8.800	0.830	29.800	32.900
Gallium	0.008	0.008	0.004	0.003	0.013	0.015
Selenium	1.020	1.590	2.060	7.710	3.810	7.860
Arsenic	0.030	0.070	0.100	0.200	0.250	0.350
Strontium	0.010	0.010	0.020	0.060	0.040	0.050
Rubidium	0.090	0.110	0.190	0.320	0.410	0.490
Ruthenium	<det	0.001	<det	0.001	<det	0.001
Palladium	0.002	<det	0.003	0.005	0.003	0.003
Cadmium	<det	<det	<det	0.002	0.005	0.003
Silver	<det	<det	0.002	0.002	0.001	<det
Tellurium	0.003	0.003	0.050	0.090	0.080	0.070

	A	B	C	D	E	F
Antimony	<det	0.002	0.003	0.002	0.007	0.006
Barium	0.017	0.019	0.035	0.040	0.057	0.080
Cesium	0.001	0.002	0.004	0.008	0.005	0.006

Note: The term <det means below level of detection.

Anion and cation analysis was also conducted on samples A-F. For this analysis, the samples were prepared as recommended in APHA Standard Methods For The Examination Of Water And Wastewater, 16th Edition, 1985 or MOE Handbook Of Analytical Methods For Environmental Samples, 1983. Instrumentation for the anion/cation analysis was: (1) for metals, Jarrell Ash 61E ICAP emission, Perkin Elmer 3030 Zeeman Graphite Furnace, and Perkin Elmer 2380 Cold Vapour AA; (2) for anions, Dionex 2000i Ion Chromatograph; and for conventionals, Skalar SA5 Segmented Flow Analyzer. The results, in mg/l, are presented in Table XI.

Table XI: Anion And Cation Analysis Of Compositions Of Example 1

	A	B	C	D	E	F
Silver	<0.007	<0.007	<0.007	<0.007	<0.007	<.007
Beryllium	<0.003	<0.003	<0.003	<0.003	<0.003	<.003
Cadmium	<0.003	<0.003	<0.003	0.004	<0.003	<.003
Bismuth	<0.04	<0.04	<0.04	<0.04	<0.04	<0.04
Cobalt	<0.005	0.005	<0.005	0.006	<0.005	<.005
Copper	0.013	0.036	0.043	0.138	0.112	0.210
Manganese	0.007	0.006	0.007	0.283	0.018	0.029
Molybdenum	0.014	0.012	0.012	0.015	<0.006	<.006
Nickel	<0.01	0.012	<0.01	0.058	0.020	0.020
Lead	<0.025	<0.025	<0.025	<0.025	<0.025	<.025
Strontium	0.01	0.019	0.015	0.126	0.040	0.063
Vanadium	0.009	0.008	0.004	0.011	<0.003	<.003
Zinc	6.04	5.93	1.95	0.383	14.5	15.2
Tungsten	0.587	0.436	0.315	0.435	0.498	0.481
Phosphorus	10.6	11.4	3.34	676	22.8	14.1
Titanium	<0.003	<0.003	0.006	0.005	<0.003	0.004
Barium	0.062	0.056	0.055	0.105	0.079	0.117

	A	B	C	D	E	F
Chromium	0.025	0.036	0.028	0.107	0.102	0.124
Sodium	1250	1570	2770	13900	5350	6570
Potassium	30.2	32.8	65.4	686	125	154
Iron	0.018	0.023	0.024	0.008	0.036	0.037
Aluminum	0.240	0.238	0.052	<0.025	0.790	0.361
Calcium	1.22	5.34	2.00	10.2	5.04	10.4
Magnesium	0.757	0.756	0.891	15.8	2.27	3.70
Fluoride	<100	<100	<100	<100	<100	<100
Chloride	2120	1860	3110	30400	10900	9110
Sulphate	144	154	152	332	1150	1590
Phosphate-P	1.8	1.3	1.5	<det	<det	<det
Nitrate as N	<10	<10	<10	<10	<10	<10
Nitrite as N	<100	<100	<100	<100	<100	<100
Bromide	<35	<35	<35	<35	<35	<35
Ammonia as N	98.0	125	130	492	425	592

As several sulfate esters participate in the regulation of many cellular events, such as cell proliferation and differentiation, Sample D was analyzed for sulfate ions before and after acid hydrolysis. Using whole sample D (i.e., unfractionated), the nonhydrolyzed sample yielded 1000 μM sulfate, whereas the hydrolyzed sample yielded 1200 μM sulfate. Since the sulfate ion concentration increased after acid hydrolysis, these results suggest that 20% of the total sulfate ions present are sulfate esters.

Physicochemical standards have been identified for the composition of Example 1 and are essentially consistent with earlier studies, which are described in Example 4. These standards indicate that a consistent product can be repeatedly obtained.

Example 4

This example describes the physical, chemical, and biological properties of a number of earlier batches of the composition of Example 1.

Batches of bile extract were prepared in accordance with the method described in Example 1. In

addition, the chemical composition of the batches was determined and an amino acid analysis of the batches was conducted, using the methods disclosed in Example 3. The results are shown in the following tables.

Table XII: Chemical Composition Earlier Batches of Compositions of Example 1

Composition Batch No.	Solids (mg/ml)	Amino Acids (μg/ml)	Sugars (μg/ml)	Lipids (μg/ml)	High M.W. >3kD Poly-peptide (μg/ml)
B0201	15.3	4.59	40.85	ND	NA
B0202	15.7	13.16	54.95	ND	NA
B0203	15.0	72.67	25.5	ND	NA
B0208	7.8	4.53	30	ND	ND
B0209	8.5	2.27	24	ND	ND
B0211	5.6	1.47	19.2	ND	ND
B0106	32.2	1.16	32.6	ND	ND
B0706	32.7	1.42	26.2	ND	ND
B1306	22.3	8.01	48	ND	ND
B2006	21.7	9.73	38.4	ND	ND
B2306	28.5	16.35	42	ND	ND
B0213	31.6	21	61	ND	ND
R0201/-pH	52.5	1553	216	ND	ND
R0201/+pH	55.8	1530	280	ND	ND
C0203	36.1	113	42	ND	ND
0-13/2109	12.1	149	36	ND	ND
B27/2806	17.5	28	37	ND	ND
B29/3006	28.7	26	60	ND	ND
B15/1606	26.8	41	45	75	ND

Note: ND means not detectable, thus less than 0.5 μg/ml lipids per and/or less than 1.0 μg/ml high molecular weight polypeptide. NA means not assayed.

Table XIII: Physical, Chemical and Biological Properties of Earlier Batches of Compositions of Example 1

Batch No.	pH	Conductance (mMho)	Osmolarity (mOsM)	Absorbance (O.D. 280 nm)	UV, VIS Peaks	Activity (Units/ml)	Potency pg/ml
B0201	7.37	16.9	361	0.98	404 nm	10.5	
B0202	7.35	17.3	298	0.777	None	6.5	
B0203	7.3	17.7	360	0.67	365 nm	21.0	
B0208	7.00	16.1	250	0.453	None	8.1	

Batch No.	pH	Conductance (mMho)	Osmolarity (mOsM)	Absorbance (O.D. 280 nm)	UV, VIS Peaks	Activity (Units/ml)	Potency pg/ml
B0209	7.31	11.2	259	0.594	None	6.7	
B0211	7.35	34.9	175	0.287	None	7.5	
B0106	7.57	34.3	627	0.341	None	17.2	
B0706	7.57	11.6	627	0.387	None	23.0	
B1306	8.02	35.6	790	1.147	None	17.0	
B2006	8.56	33.9	651	1.024	None	21.0	
B2306	8.01	35.1	623	1.054	None	19.0	
B0213	7.75	29.5	628	0.48	none		858
R0201-pH	7.95	44.5	877	1.59	271 nm 0.65 O.D.		NA
R0201/-+pH	7.60	50.0	1162	2.29	266 nm 1.6 O.D.		NA
C0203	7.90	34.8	657	0.96	none		NA
0-13/2109	7.73	17.0	316	0.83	none		NA
B27/2806	7.71	22.0	453	0.49	none		NA
B29/3006	7.67	28.8	605	0.55	none		NA
B15/1606	7.84	35.0	753	1.04	none		NA

Comments:
1. Full isotonic PBS solids were added to batches No. B0106 and B0706 .
2. Batches B1306, B2006 and B2306 were concentrated two times without adjusting pH.

Table XIV:
Amino Acid Composition of Earlier Batches of Composition of Example 1

	BATCH NUMBER							
	B-0208	B-0209	B-0211	01/06	07/06	1306	2006	2306
Asparagine	365				113			289
Serine		69	12	7	17	144	119	308
Glycine	22	449	274	279	417	3731	5314	10371
Histidine		192		90	68	938	1335	2114
Arginine				161		533		
Threonine		19	13		30	148	142	250
Alanine		173	112	24	64	949	1002	1423
Proline	1092				74	817	639	1075
Tyrosine	15	55	57	43	39	205	135	45
Valine	121	63	31	10	15	367	335	224
Methionine		970	461	462	13	107	121	70
Cysteine		103	90	41	12	86	49	10
Isoleucine	2721	84	95	17		232	216	68
Leucine		58			9	221	242	84
Phenylalanine		57	200	16		45	80	23
Lysine	191	36	123	6	18		15	
Total AA µg/ml	4.53	2.27	1.47	1.16	1.42	8.01	9.73	16.35

Example 5

This example describes the biological activity of fractions of the composition of Example 1.

The biological activity of fractions of the composition of Example 1 was investigated. The analytical results are consistent with the biological activity of the composition being attributed to small molecular weight components (i.e., less than 3000 daltons). This was determined through an experiment in which the composition was passed through the reverse-phase HPLC described in Example 3 and eluted fractions who isolated and analyzed for potency by the PBMN-TNF assay described in Example 2. Significant activity was only detected in the early-eluting peak (F1), i.e., 5.6 to 6.2 mins. which is consistent with a molecular weight of less than 3000 daltons (see Table XV).

Table XV: Effect of Fractions of Composition of Example 1 Eluted by Reverse-Phase HPLC on TNF Release From LPS-Induced PBMNs

Sample Tested	HPLC (min)	Quantity per Well	TNF-α Released (pg/ml) Total	-LPS	Osmolarity (mOsm)
LPS	-	50 ng	305 ± 79	0	304
Composition of Example 1:					
Whole	0	100 μl	519 ± 195	213	415
F1	5.60-6.20	100 μl	508 ± 82	203	344
F2	6.20-6.55	100 μl	149 ± 44	-157	281
F3	6.55-7.10	100 μl	306 ± 80	1	309
F4	7.10-7.90	100 μl	316 ± 123	11	309
F5	7.90-8.40	100 μl	390 ± 95	84	309
F6	8.40-8.90	100 μl	282 ± 103	-24	311
F7	8.90-9.40	100 μl	296 ± 108	-10	309
F8	9.40-10.00	100 μl	341 ± 112	36	309
F9	10.00-10.40	100 μl	33 ± 139	24	308
F10	10.40-12.00	100 μl	316 ± 101	11	311
F11	12.00-13.60	100 μl	354 ± 74	49	311
F12	13.60-14.20	100 μl	344 ± 107	39	315
F13	14.20-15.35	100 μl	296 ± 117	-9	311
F14	15.35-15.75	100 μl	344 ± 108	39	314
F15	16.75-18.20	100 μl	300 ± 104	-5	313

Note:

1. Number of patients tested: 3.
2. Total TNF-a Released is corrected for release by RPMI Media (13 ± 4 pg/ml, 306 mOsm).
3. HPLC fractions 1-2 reconstituted in water; 3-15 reconstituted in PBS buffer.
4. Columns in tandem are: W-Porex C18 and PrimeSphere. Both from Phenomenex, 250 x 4.6 mm.
5. Volume of LPS per well: 10 μl.
6. Total volume per well: 1000 μl.
7. Sample volumes are equivalent.

Additional experiments were done as follows to show that the active (TNF-releasing) components had molecular weights less than 3500 and less than 1000 daltons. Batch BC0241 was fractionated by carrying out a Folch extraction according to Tamari et al., Agr. Biol. Chem., 40 (10), 2057-

2062 (1977). The water layer was dried on a rotovap to yield a light brown, granular solid. A stock solution of this solid was prepared at a concentration of 5 mg/ml. A portion of the stock solution was loaded into Centri/por Centrifuge Concentrators (Spectrum Products, Houston, TX) having a 3500 or 1000 dalton molecular weight cutoff membrane. The Concentrators were centrifuged at approximately 1500 x g until a portion of the material had passed through the membrane. The solution that passed through the membrane was assessed for potency in the PBMN-TNF assay. The results are presented in Table XVI.

Table XVI: Molecular Weights of Active Components of Composition of Example 1

SAMPLE	TNF Released (pg/ml)
Folch water layer from BC0241	1709
Folch water layer passed through 3500 dalton membrane	2318
Folch water layer passed through 1000 dalton membrane	2423

The analysis of the biological activity of molecular weight fractions indicates, accordingly, that the TNF-releasing components are less than 1000 daltons molecular weight.

Example 6

This example illustrates the effect of the composition of Example 1 on T and B lymphocytes in culture.

The growth of human lymphocytes was examined under carefully controlled conditions in the presence and absence of the composition of Example 1. Standard concentrations of lymphocytes were incubated in wells containing various concentrations of the composition. When normal T and B human lymphocytes were incubated with the composition in concentrations similar to those that are used clinically, there were no adverse effects as judged by trypan blue dye exclusion. Accordingly, the composition of the invention was non-toxic to normal T and B lymphocytes in culture.

The effect of the composition on the survival of human PBMN also was examined. PBMNs were incubated for 24 and 48 hrs in plastic microwell plates with various volumes of the composition and tissue culture medium. At the end of this period, the number of surviving cells was estimated

by trypan blue dye exclusion.

Table XVII: Concentration of Viable PBMNs

After Incubation with Composition of Example 1

		No. of Live PBMN per Well by Trypan Blue ($x10^6$)[1]	
Concentration (µl/well)	Zero time	After 24 hrs No. (% viable)	After 48 hrs No. (% viable)
Patient S.Z.			
0	0.70[2]	0.23 (33)	0.10 (14)
25		0.43 (61)	0.15 (21)
50		0.10 (14)	0.23 (33)
100		0.15 (21)	0.18 (26)
200		0.48 (69)	0.23 (33)
LPS (µg/well)			
1		0.30 (43)	0.28 (40)
10		0.25 (36)	0.13 (18)
Patient E.S.			
0	1.30[2]	0.70 (54)	0.33 (25)
25		0.65 (50)	0.15 (12)
50		0.68 (52)	0.38 (29)
100		0.75 (58)	0.23 (18)
200		0.65 (50)	0.20 (15)
LPS (µg/well)			
1		0.60 (46)	0.53 (41)
10		0.15 (12)	0.15 (12)

[1] Approximately 1 x 10^6 cells plated/well in triplicate.
[2] Actual number of cells counted/well ($x10^6$).

The above data show that the number of surviving cells fell at 24 and again at 48 hours; however, the number of surviving cells in the presence or absence of the composition was not different. Moreover, increasing volumes of the composition had no effect on survival. Thus, the composition showed no cytotoxicity to human PBMN..

The ability of the composition to stimulate lymphocytes was evaluated in the following 3 indicator systems: 1) stimulation of lymphocyte DNA synthesis; 2) induction of lymphocyte-mediated cytotoxic function; and 3) induction of monocyte/macrophage-mediated cytotoxic function. These

tests were chosen for the screen because they measure immunological functions that have been shown to be associated with different clinical parameters in patients with malignant disease. These indicators of immune function also can be modulated in cancer patients treated with different biological response modifying agents, such as IFN or IL-2. The results of the initial screening procedures are presented below.

1. Stimulation of lymphocyte DNA synthesis: comparison with an optimal stimulating concentration of phytohemagglutinin (PHA):

Stimulant	Counts Per Minute
Medium	374
PHA	125,817
Composition (#222)	1,116
Composition (1:10)	1,021
Composition (1:50)	649

Unlike the prototypic mitogen, PHA, it was noted that the composition of Example 1 did not stimulate lymphocytes to undergo blastogenesis and cell division, which is consistent with these results showing little or no stimulation of DNA synthesis by the composition.

2. Stimulation of lymphocyte-mediated cytotoxic function and comparison with an optimal stimulating concentration of IL-2:

Stimulant	Lytic Units
Medium	30.8
IL-2	472.5
Composition (neat)	48.1
Composition (1:10)	33.3
Composition (1:50)	44.8

Unlike the prototypic stimulator of lymphocyte cytotoxic function, IL-2, the composition did not elicit lymphocyte cytotoxicity. The number of lytic units stimulated by the composition was virtually identical to that of the negative control (i.e., medium).

3. Stimulation of monocyte-mediated cytotoxic function by the composition: comparison with IFN-γ and LPS (IFN + LPS)

Stimulant (E/T=20/1)	% Cytotoxicity
Medium	4.3
IFN+LPS	24.4
Composition (neat)	19.7
Composition (1:10)	20.0
Composition (1:50)	11.5

The composition of Example 1 was capable of stimulating peripheral blood monocytes to express tumoricidal function in a dose-dependent manner. The magnitude of stimulation is comparable to that elicited by the prototypic macrophage activator combination of IFN-γ and LPS. It is important to recognize that the action of the composition in these *in vitro* assays did not require the addition of endotoxin, as in the case with any other macrophage activator.

Example 7

This example illustrates the results of assays conducted to survey what, if any, cytokines are present in the composition of Example 1.

Samples of a bile extract (50 µl and 100 µl aliquots per test) prepared according to Example 1 were tested for the presence of the following cytokines (sources and detection limits of the ELISA immunoassay kits used are noted parenthetically): TNF-α (Endogen, Inc. (5 pg/ml)); IL-1α (Endogen, Inc. (50 pg/ml)); IL-1β (4.3 pg/ml); GM-CSF (Endogen, Inc.); RFN-α (Endogen, Inc.); IL-2 (Advanced Magnetics, Inc.); IL-6 (Advanced Magnetics, Inc. (7 pg/ml)); IFN-γ (5 pg/ml)[source]; IL-1 (Advanced Magnetics, Inc.) [need limit]; IL-4 (R&D Systems (3 pg/ml)); and IL-8 (R&D Systems (4.7 ng/ml)). Procedures used were according to the individual kit's instructions, which can be easily followed by an ordinary artisan.

It was determined that the composition of the invention contained no measurable levels of any cytokine tested, those being TNF-α, IL-1 α, IL-1 β, IL-4, IL-6, IL-8, GM-CSF and IFN-γ, as described in Table XVII.

Table XVIII: Elisa Determination of Cytokines In Composition

Cytokine (pg/ml)	50 μl	100 μl
TNF	<5	<5
IL-1β	–	6.5
GM-CSF	<5	–
IL-6	<7	–
IFNγ	<5	–
IL-1α	<50	–
IL-4	–	<3
IL-8 (ng/ml)		<4.7

Example 8

This example describes pharmacodynamic studies in mice with the composition of Example 1, including the direct *in vitro* effect of Virulizin™ as well as the effect of Virulizin™ administered *in vivo* on murine peritoneal macrophages.

Peritoneal macrophages were harvested from C57BL/6 mice 72 hours after intraperitoneal injection of 1.5 ml of 4% protease peptone. The macrophages were then stimulated *in vitro* with medium alone, 50 ng LPS, or VIRULIZIN™. Measurements of the stimulation was done with respect to TNF (by ELISA) and NO (by spectrophotometric assay using the Greiss reagent) levels in duplicate experiments. Standard error of the mean between duplicate experiments was less than 10%. As noted in Table XIX, VIRULIZIN™ induced a slight increase in TNF-α production (60-232 pg/ml) compared to background (medium) levels (120 pg/ml), but VIRULIZIN™ in comparison to LPS (2225 pg/ml) was not a strong stimulant of macrophage TNF-α release. Nitric oxide production was zero.

Table XIX: In Vitro Stimulation of Protease Peptone Macrophages

Macrophages Stimulated With	TNF (pg) Mean	NO (μM) Mean
Medium	120	0
LPS (1 μg/ml)	2225	11
Virulizin		
1:2	62	0

1:5	181	0
1:10	206	0
1:20	202	0
1:40	232	0
1:80	142	0
1:200	122	0

In vitro synergy of Virulizin™ with LPS for TNF-α release was also addressed. Peritoneal macrophages were harvested from C57 L/6 mice after the same aforementioned treatment. The macrophages were then stimulated with 50 ng LPS alone or LPS with different dilutions of VIRULIZIN . As above, TNF was determined via ELISA. As noted in Table XX, LPS alone induces about 2900 pg/ml of TNF-α release from mouse peritoneal macrophages *in vitro* compared to 262 pg/ml for medium. When LPS is combined with VIRULIZIN , there is about an 800 pg/ml increase in TNF-alpha release at dilutions of VIRULIZIN 1:5 and 1:10 and enhanced release to at least 1:40.

Table XX: Synergistic Combinations between Virulizin™ and IFN-α or LPS

Macrophages Stimulated With	TNF (pg/ml)	NO (μM)
Medium	262	1.6 ± 1.1
LPS (5 ng/ml)	2900	8.6 ± 1.3
LPS (5 ng/ml + Composition of Example 1:		
1:5	3750	13.2 ± 0.5
1:10	3750	16.9 ± 2.7
1:20	3500	13.5 ± 2.5
1:40	3600	27.1 ± 11.6
1:80	3000	10.1 ± 1.9
1:200	3400	9.7 ± 1.3
1:1000	3200	9.4 ± 1.2
IFN-γ (100U)+LPS (5 ng/ml)	6800	74.1 ± 0.6
IFN-γ (100U)+Virulizin:		
1:5	512	46.9 ±0.6
1:10	625	57.3

In vitro synergy of Virulizin™ with LPS for nitric oxide (NO) was addressed in the same procedure as above, except NO was determined in the supernatant of the treated macrophages. As above, the assay for NO is spectrophotometric and uses a Greiss reagent. As noted in the table above, LPS causes some release of NO (9 μM). VIRULIZIN in synergy with LPS induces a marked increase in NO production (13-27 μM) to dilutions of 1:40. VIRULIZIN by itself did not induce release of NO by macrophages.

In vitro synergy of Virulizin™ with IFN-γ for TNF-α release was studied, using the same peritoneal mouse macrophages derived from C57 L/6 mice treated as above. The data are included in the table above concerning "Synergistic Combinations." As shown, peritoneal mouse macrophages exhibit a baseline release of TNF-α after 24 hours of *in vitro* culture. The same macrophages stimulated with either LPS or IFN-γ release almost 3000 pg/ml of TNF-α. When VIRULIZIN and IFN-γ were added together, the release of TNF-α was diminished. y comparison, the combination of LPS and IFN-γ have an additive effect on TNF-α release.

In vitro synergy of Virulizin™ with IFN-γ for NO release was studied, using the same peritoneal mouse macrophages derived from C57 L/6 mice treated as above. The data are included in the table above concerning "Synergistic Combinations." As shown, LPS and IFN-γ alone each enhanced NO production (9 and 7 μM, respectively). VIRULIZIN added to IFN-γ induced a marked increase in NO production (47-57 μM) that almost equaled the combination of LPS and IFN-γ (74 μM). The results are consistent with the conclusion that VIRULIZIN in combination with IFN-γ enhances NO production but inhibits TNF-α release.

In vivo production of TNF-α over 72 hours was studied on macrophages harvested from C57 L/6 mice that, prior to harvest, were treated with nothing, in ected intraperitoneally 72 hours previously with 1.5 and 4% protease peptone, or in ected intraperitoneally 72, 48, or 24 hours previously with 1.0 ml Virulizin™ diluted 1:10 in P S. The macrophage monolayers were treated *in vitro* for 24 hours with IFN-γ (50 μ/ml), LPS only (5 ng/ml), or the combination thereof. TNF and NO were determined as recited above. The data are presented in Table XXI.

Table XXI: TNF and No Release From Macrophages Harvested From Treated Mice

Macrophages Harvested from Mice Injected With	*In Vitro* Stimulant	TNF (pg/ml)	NO (μM)
Nothing	Medium	315	0
	IFN-γ	402	25.8 ± 1.6
	LPS	3,750	1.9 ± 0.2
	IFN-γ+LPS	6,300	40.9 ± 3.8
Protease Peptone (72 hrs prior)	Medium	335	0.9 ± 0.5
	IFN-γ	838	48.6 ± 1.7
	LPS	5,975	23.2 ± 3.4
	IFN-γ+LPS	10,875	55.8 ± 1.9
Virulizin (72 hrs prior)	Medium	258	1.2 ±0.6
	IFN-γ	425	37.5 ± 2.6
	LPS	3,300	4.0 ± 0.9
	IFN-γ+LPS	4,650	54.0 ± 0.9
Virulizin (48 hrs prior)	Medium	350	8.5 ± 1.8
	IFN-γ	560	62.0 ± 2.5
	LPS	5,300	36.5 ± 1.2
	IFN-γ+LPS	12,475	58.5 ± 1.6
Virulizin (24 hrs prior)	Medium	248	2.9 ± 2.1
	IFN-γ	475	44.1 ± 0.7
	LPS	9,025	12.5 ± 2.4
	IFN-γ+LPS	12,375	52.8 ± 0.6

As described, the release of TNF-α from macrophages was examined in the absence of a stimulus or with IFN-γ, LPS, or LPS/IFN-γ after 24 hrs *in vitro* culture. Mouse peritoneal macrophages were shown to release little TNF-α after *in vivo* stimulation with VIRULIZIN™. When the harvested macrophages were exposed to IFN-γ at 24 and 48 hrs prior to testing, they showed a small increase in production of TNF-α. By contrast, harvested macrophages stimulated with LPS at 24 and 48 hrs, but not 72 hrs prior to testing, showed enhanced release of TNF-α. Likewise, there was a synergistic effect of LPS and IFN-γ on harvested macrophages that were stimulated 24 and 48 hrs but not 72 hrs before testing.

In vivo production of NO over 72 hrs was studied with macrophage cells and tests under the same conditions described above with respect to TNF-α production. There was a small spontaneous release of NO measured at 24 and 48 hrs after intraperitoneal injection of VIRULIZIN™

(hereinafter IP Virulizin™). When the harvested cells were incubated with IFN-γ, there was a marked release of NO, and the harvested macrophages that had IP VIRULIZIN™ at 24 and 48 hrs prior to testing showed an exponential increase in release of NO, which fell back at 72 hrs towards the baseline values of IFN-γ alone. When the harvested cells were stimulated with LPS, they showed a markedly enhanced output of NO, which was once again observed for the 24 and 48 hrs VIRULIZIN™-treated macrophages compared to macrophages that had not received IP VIRULIZIN™. The harvested macrophages that had received IP VIRULIZIN™ 72 hrs before responded no differently than macrophages that had no VIRULIZIN™ pretreatment. Finally, when harvested macrophages pretreated with IP VIRULIZIN™ were incubated with LPS/IFN-γ, they showed enhanced production of NO compared to macrophages not so pretreated. The maximum response was with macrophages pretreated with VIRULIZIN™ 48 hrs before harvesting and testing.

Example 9

This example illustrates the results of assays conducted to estimate protein within the composition.

Protein estimation of the composition was done using the Pierce Micro BCA Protein determination technique (Smith et al., Anal. Biochem., 150, 76-85 (1985)). A 10 μl sample of a batch of the composition was made up to 1 ml with distilled water. Five concentrations of bovine serum albumin (0.150 μg/ml) was also made up to be used as standards. As a blank, O.1 N NaOH was used. To all these samples was added a mixture of BCA (2% bicinchonic acid sodium salt; Pierce), 4% copper sulfate and microreagent A ($NaCO_3$, $NaHCO_3$, Na tartrate in 0.2N NaOH). The sample mixtures were incubated for 1 hr at 60°C, cooled, and the resultant absorbency read at 562 nm using a spectrophotometer. The amount of protein in the test sample was then compared to the plotted standard curve and the appropriate calculations made. The protein concentration of the composition was found to be low and estimated to be 32 μg/ml.

Example 10

This Example demonstrates, in summary, the following: (1) the composition has TNF-α releasing activity and the TNF-α releasing activity is not related to any contamination with endotoxin; (2) priming of macrophages enhances the ability of the composition to stimulate release of TNF-α; and (3) the hyperosmolarity of the composition is not responsible for TNF-α releasing activity.

To test whether an endotoxin effect was associated with the biological activity noted above for the composition of Example 1, further composition experiments were performed with polymyxin added to the reactants. Polymyxin inhibits the action of endotoxin on leukocytes. The following table and succeeding notes recite the composition experiment performed and its results.

Table XXII: Absence of Endotoxin for TNF-2 Releasing Effect and Enhancement of Release With Macrophage Priming

		TNF Released (pg/ml)	
Sample Tested	Additive	Total	-LPS
LPS	Polymyxin	11 ± 7	0
	None	517 ± 118	0
Composition (#B02-13)	Polymyxin	1591 ± 413	1581
	None	5256 ± 2585	4738

Notes:
1. Total TNF released is correct for TNF release by 1640 medium.
2. Polymyxin concentration: 50,000 units/ml.
3. Composition volume: 200 μl.
4. With polymyxin, 8 patients tested. With no additive, 3 patients tested.
5. LPS concentration: 50 ng/10 μl.

The results show that polymyxin completely inhibits the LPS-induced release of TNF-α. In the absence of polymyxin, LPS induces 517 pg/ml of TNF-α, whereas in the presence of polymyxin, 11 pg/ml of TNF-α is released. The composition, on the other hand, releases 1591 pg/ml of TNF-α in the presence of polymyxin. In the absence of polymyxin, LPS and the composition show more than just an additive effect of the stimulators, suggesting that the composition acts with greater intensity when macrophages are primed.

Table XXIII: Absence of Effect of Hyperosmolarity on TNF-2 Release

Batch #	pH	Osmolarity (mOsm)
Concentrated:		
B0222	pre-pH	411
B0222	pH adjusted	581
B0216	pH adjusted	872
B0219	pH adjusted	886

Batch #	pH	Osmolarity (mOsm)
Nonconcentrated:		
B0221	pre-pH	652
B0221	pH adjusted	533
B0213	pH adjusted	675
B0225	pH adjusted	590
B0226	pH adjusted	540
BC 11-06	pH adjusted	445
BC 11-09	pH adjusted	603

The osmolarity of different batches was determined using standard methods. The results are shown in the previous table. B0213 is moderately high at 675 mOsm. B0222, shown to have TNF releasing activity even better than B0213, is less hyperosmolar, 581 mOsm. The fractions B0226, BC11-06 and BC11-09 range from 540 to 603 mOsm. The effect of the hyperosmolarity of the composition on TNF-α releasing activity was also studied. It was found that the composition, when adjusted for osmolarity, even to the point of being hypoosmolar, continued to release TNF-α.

Example 11

This example illustrates toxicity studies regarding the composition of the present invention. Preliminary toxicity studies were conducted on a variety of animal species, as tabulated below.

All animals (listed in the following table) were assessed on the basis of daily clinical observation while receiving the injections of the composition on days 14, 21 and 30 thereafter. Hematologic data was collected every third day for the first 30 days and once monthly thereafter. No adverse effects were noted in any of the over 358 animals included in this study throughout the period that injections were administered or during the follow-up period (one month for all species except the dogs which were followed for 4 months).

Animal	Quantity	Dose
White mice	100	0.2 ml i.m. at 3-day intervals 4 times
Male Wistar rats	100	2.0 ml i.m. at 3-day intervals 4 times
Golden hamsters	60	1.5 ml i.m. at 4-day intervals 4 times

Guinea pigs	60	3.0 ml at 3-day intervals 4 times
Rabbits	15	5.0 ml i.m. at 3-day intervals 4 times
Cats	10	3.0 ml i.m. at 3-day intervals 6 times
Dogs	12	2 ml/kg i.m. given once - observed for 4 months

A second toxicity study was conducted to determine the effect of a single large intramuscular dose of the composition. Thirteen Sprague Dawley rats received a single intramuscular dose of 5 ml/kg of the composition. Three rats were observed for 7 days. Ten rats were observed for 14 days followed by euthanasia and necropsy. No symptoms of toxicity were observed in either group and no gross pathologic findings were observed in the animals that were necropsied. Based on these observations the LD_{50} for intramuscular administration of the composition in rats was determined to be greater than 5 ml/kg.

Another toxicity trial was conducted by the Ontario Veterinary College, wherein the composition was administered to two mixed breed dogs. The protocol is summarized in the following table:

Animal	Age and Weight	Dose 1	Dose 2	Dose Interval
Male Mixed Breed	Adult 5 kg	5.5 ml i.m.	0.6 ml i.m.	7 days
Female Mixed Breed	6 months 13 kg	12.5 ml i.m.	1.3 ml i.m.	7 days

In each case, one dose was given in the right rear leg and the second dose 7 days later was given in the left rear leg. Both dogs were observed for 14 days after the first injection. Appetite, activity, temperature, pulse rate, and respiratory rate were monitored twice daily throughout the study. Routine urinalyses, hematology and serum chemistry profiles were performed at the following time points: pretreatment and 24 hours, 72 hours, 7 days and 14 days after the first injection. Neither animal showed signs of pain associated with either injection. There was no evidence of anaphylaxis associated with the second injection. No abnormalities or changes in physical or laboratory parameters were observed that could be attributed to the drug. The drug appeared to be well tolerated by healthy dogs.

A 17-day repeat dose toxicity study was carried out with VIRULIZIN™ in conjunction with an animal model study at the Ontario Cancer Institute. The model used female C57Bl mice.

There were 4 groups as follows (IM = intramuscular, IP = intraperitoneal):

Group #	Treatment	Dose Volume	Number/Group
1	Saline, IM	0.05 ml	10
2	Virulizin™, IM	0.05 ml	10
3	Virulizin™, IM	0.05 ml X2	10
4	Virulizin™, IP	0.5 ml	10

Each group of mice were injected at day 0 with 5 X 10^3 of B16F1 melanoma cells plus microspheres. On each of the first 17 days, each group received daily injections of Virulizin™ or saline, as above. On day 18, the animals were sacrificed.

Prior to sacrifice, food intake, weight gain, and behavior were normal. In addition, there was no evidence of toxicity causing changes observable by light microscopy in any of the organs examined, which were: large intestine, spleen, stomach, pancreas, urinary bladder, liver, brain, kidneys, small intestine, and heart. Food intake and behavior were normal. Weight gain was normal.

A 13-week repeat dose toxicity study in Fischer-344 rats (total of 40 males and 40 females) was carried out administering VIRULIZIN™ IM three times per week for 13 weeks. The largest dose was 1.1 ml/kg, about 20 X the human dose. Animals were subjected to full histopathology after 13 weeks. The only treatment related finding observed was a small decrease in mean body weight gain in the 20 X dose group as compared to controls. No toxicity was demonstrated.

Example 12

This example illustrates the isolation of active fractions.

A 300 ml sample of the composition was evaporated to dryness on a rotovap in which the temperature of the bath did not exceed 40°C. In order to ensure that the solution remained basic during the evaporation, 5 drops of a concentrated ammonium hydroxide solution was added every half hour to the composition until the evaporation was complete. The resulting residue had a weight of 11.6g.

20 ml of a 10% concentrated ammonium hydroxide in methanol solution was then added to 2 g of the above residue. The insoluble material was filtered off and the filtrate was chromatographed through 101.93 g of 60Å flash silica gel in a column with dimensions of 5 cm x 12.5 cm. The solvent system used was 10% concentrated ammonium hydroxide in methanol solution. The column was run at a pressure of 10 p.s.i. and a flow rate of 11 ml/min. After 100 ml of solvent had passed through the column, twelve 20 ml. fractions were collected. The collection of these fractions correlated to the appearance of an off-white band that was quickly moving down the column.

Thin layer chromatography (TLC) of these fractions was run on silica gel plates in a 10% concentrated ammonium hydroxide solution in methanol and visualized with a ninhydrin spray. Fractions having similar TLC profiles were combined, resulting in the following fraction combinations, which were dried on a rotovap:

Fractions	Volume Through Column to Obtain Fraction	Yield (g)
1-4	100-180	0
5-6	180-220	0.1175
7-8	220-260	0.1969
9-10	260-300	0.0151
11-12	300-340	0.0053

Fractions 5-6, 7-8 and 9-10 had a positive reaction with ninhydrin at an R_f value of 0.81.

Fractions 5-6 and 9-10 were tested *in vitro* for TNF stimulation (in accordance with Example 19). The results are shown below:

Fraction	Activity
5-6	50 pg/mg
9-10	1814 pg/mg

Thus, fraction 9-10 was an extremely active TNF stimulator.

Samples of Fraction 5-6 were analyzed by Electron Impact Mass Spectroscopy (EI MS) and Electrospray Mass Spectroscopy to identify specific compounds likely to be present in the fraction. The Electrospray MS was performed on a Perkin-Elmer Sciex API-III spectrometer, using 5% acetic acid in water as the solute. In some instances, methanol was added to aid dissolution. The EI MS using a direct insertion probe was performed on a VG Analytical model ZAB-SE spectrometer using glycerol as a matrix, and using a DCI probe on a Kratos Analytical Profile Mass Spectrometer.

A review of the resultant spectra indicated that the following compounds were likely present in Fraction 5-6: phosphocholine, taurocholic acid, choline-stearic acid diglyceride, stearic acid, stearic acid diglyceride, palmitic acid-stearic acid diglyceride, and a sphingosine-oleic acid conjugate.

Example 13

This example illustrates an expanded procedure to isolate active fractions.

Example 12 was repeated on a larger scale, as follows. 10 ml of a concentrated ammonium hydroxide solution was added to 900 ml of the composition and the resulting solution evaporated to dryness on a rotovap in which the temperature of the bath did not exceed 40°C. In order to ensure that the solution remained basic during the evaporation, 5 drops of a concentrated ammonium hydroxide solution was added every half hour to the composition until the evaporation was complete, leaving a residue.

150 ml of a 10% concentrated ammonium hydroxide in methanol solution was then added to the total residue. The solution was sonicated for 15 min. and the insoluble material was filtered off. The filtrate was chromatographed through 1695g of 60Å flash silica gel in a column with dimensions of 30cm x 12cm. The solvent system used was 10% concentrated ammonium hydroxide in methanol solution. The column was run at a pressure of 6 p.s.i. and a flow rate of 30 ml./min. The results of the column are summarized in the table below.

Fraction #	Volume of each fraction (ml.)	Observations
1	550	clear, yellowish

Fraction #	Volume of each fraction (ml.)	Observations
2	450	clear, yellowish
3	400	clear, yellowish
4	150	clear, yellowish
5	100	clear, yellowish
6-7	75	clear, yellowish
8-13	50	clear, yellowish
14	50	tan colored solution begins to elute
15-35	50	tan colored solution
36-40	50	clear, yellowish

TLC was run on silica gel plates in a 10% concentration ammonium hydroxide solution and visualized with a ninhydrin spray. Fractions having similar TLC profiles were combined, resulting in the following fraction combinations, which were dried on a rotovap:

Fraction #	Volume Through Column to Obtain Fraction	Yield (g)	Comments
3	1000-1400	0.0504	white powdery solid
4-5	1400-1650	0.0855	white powdery solid
6-8	1650-1850	0.1555	white powdery solid
9-12	1850-2050	0.3014	white powdery solid
13-14	2050-2150	0.3595	white powdery solid
15-16	2150-2250	0.6914	slight brown color - solid is tacky
17-18	2250-2350	1.0284	tan color - solid is clumpy
19	2350-2400	0.3432	tan color - solid is clumpy
20-23	2400-2600	1.1531	brown color - solid is clumpy
24-30	2600-2950	0.8517	brown color - solid is clumpy
31-34	2950-3150	0.0813	brown oil

All fraction combinations from 15-16 through Fraction 31-34 had a positive reaction with ninhydrin at an R_f value of 0.87, a value very similar to the R_f value for the active fractions of Example 28. Fractions 24-30 and 31-34 had an additional positive reaction with ninhydrin at an R_f value of 0.85.

Fractions 4-5, 15-16 and 17-18 were tested *in vitro* for TNF stimulation (in accordance with Example 19), resulting in no TNF stimulation activity. Elemental analysis of the above fractions showed them to be high in NH_4Cl, which is known to inhibit TNF production.

Samples of fractions 15-16 and 24-30 were dialyzed and then analyzed by mass spectroscopy, using the methods described in Example 12. Undialyzed samples from fractions 17-18 and 24-30 were also analyzed. A review of the resultant spectra indicated that the following compounds were likely present: glycocholic acid, a trihexosamine trimer, and taurocholic acid (Fraction 15-16); stearic acid, and a hexosamine dimer; and glycocholic acid (Fraction 24-30).

Example 14

This example illustrates the application of further methods to fractionate and analyze the active components of the inventive composition.

Having identified that TNF, IL-1β and GM-CSF releasing activity can be precipitated, in part, by 80% acetonitrile and that much of the releasing activity elutes early from C_{18} RP-HPLC, the physicochemical properties of the precipitate fraction have been studied and compared to the whole composition and supernatant fraction of the composition.

Figure 6 shows an SDS gel electrophoresis of whole composition and precipitates and supernatants of the composition. In all three instances, the composition runs near the SDS front, indicating a low molecular weight. The smallest standard used was 14,400 daltons.

The molecular size of the composition was also examined by determining its time of elution from a molecular sieve HPLC column. The elution times of whole composition, precipitate and supernatant compared to standards. All three eluted later than insulin, which eluted at 24.5 min. Once again, physicochemical analysis indicates a mol. wt. less than 2,400 daltons.

The TNF-releasing component elutes early. Thus a column with the opposite effect was chosen, a hydrophilic column in the presence of organic solvents. The ideal eluting conditions for the polyhydroxyethyl column is 80% acetonitrile. However, as indicated in the prior Example, some of the substances in the preparation precipitated at this concentration. Consequently, the composition was analyzed at a low concentration of acetonitrile where the column functions mostly as a molecular sieve column. Figures 7 and 8 show the profile of whole supernatant and precipitate. The front sheet summarizes the elution time for the different peaks. The elution times indicate the active component of the composition has a low molecular weight.

The composition and its precipitate and supernatant were separated by ion-exchange HPLC. Both by AX300 (anion exchange) chromatography and by CMX 300 (cation exchange) chromatography, there was no significant separation of components. Hydrophobic reverse phase chromatography did not separate the peaks.

In another series of experiments, 10 ml of VIRULIZIN™ was loaded onto an anion exchange chromatography column (Bio-Rad AG-1, hydroxide form, total resin wet volume was 10 ml, equilibrated with Millipore deionized water). The volume of resin was calculated to be sufficient for the binding of all the anions present in the extract. The unbound fraction was collected and reloaded onto the column in order to maximize the binding to the resin. The unbound fraction from this second passage was collected and saved. Any unbound material remaining on the column's void volume was removed by washing with deionized water (2 X 20 ml). Bound molecules were eluted with a step gradient of ammonium bicarbonate, 20 ml/step. Free ammonium bicarbonate was removed by lyophilization. Samples from all the fractions were tested for TNF-releasing activity in the monocyte/macrophage activation assay. TNF-releasing activity was not found in the unbound fraction (effluent), but the majority was found in the eluate eluted with 0.2 M ammonium bicarbonate. These results indicate that the active components are polar, anionic, acidic in nature.

Samples from all the fractions were analyzed for TNF stimulation activity, in accordance with the procedures of Example 2. The results are shown below:

Sample	TNFα release-inducing activity-LPS (pg/ml)
0 M	-496
0.1 M	-156
0.2 M	1638
0.3 M	-36
0.4 M	256
0.5 M	-27
0.6 M	-175
1.0 M	-246
1.5 M	-346
VIRULIZIN™ control	1961

The results from the activity assays show that TNF production stimulation was found in the 0.2 M and 0.4 M fractions.

The composition was subjected to dialysis and drying of the dialysate, as follows: 100 ml of the composition was placed inside a Spectra/Por® CE membrane tubing which had a molecular weight cut off of 100. The ends of the tubing were sealed with clips and the tubing was placed into a stirred bath of 10 L of distilled water. The dialysis was monitored daily by removing 1 ml. of solution from the dialysis tubing and adding 3-4 drops of a 1/10 N silver nitrate solution. The presence of chloride indicated that the dialysis was not complete. If the dialysis was not complete the bath was replaced with fresh distilled water. Dialysis completion occurred after 3-4 days. After dialysis was complete, the dialyzed material was dried on a rotovap to yield an average of 0.3 mg of solid per ml of original volume.

A sample of the solid material was then dissolved in HPLC grade water, and TLC was run on silica gel plates in a 10% concentrated ammonium hydroxide solution in methanol, and visualized with a ninhydrin spray. A positive reaction with ninhydrin was obtained at an R_f value of 0.83.

A sample of the solid material was also analyzed by mass spectroscopy, using the methods described in Example 12. A review of the resultant spectra indicated that the following compounds were likely present: a sphingosine-oleic acid conjugate, diacetyl sialic acid, a fucose-

hexosamine dimer, deoxyglycocholic acid, taurocholic acid, a sialic acid-fucose dimer, and a di(fucose)hexosamine trimer.

Example 15

This example will illustrate the use of Reverse Phase - HPLC (RP-HPLC) to analyze the inventive composition.

Samples were lyophilized and then reconstituted in 0.1% trifluoroacetic acid (TFA) in water (buffer A) and subsequently run in the following columns and conditions:

Column:	WP60009-C18 column (W-Pore C18, 250 X 4.6 mm, Phenomenex, California) in row with prime-sphere HC-C18 column (250 X 4.6 mm, Phenomenex, California)
Eluents:	Buffer A:0.1%TFA in H_2O
	Buffer B:0.1%TFA in acetonitrile
Gradient:	150 μl sample applied to column
	Run buffer A for 20 minutes
	Start linear gradient, 0-80% buffer B, run over 35 minutes
	Run 80-0% buffer B over 5 minutes
Flow:	0.9 ml/minute
Temperature:	Ambient
Detection:	Absorbance from 290 to 284 nm, with most runs being detected at 210 and 235

Fifteen eluent fractions were collected, at the approximate times from injection noted in the following table. In addition, a TNF release essay, as described in Example 2, was performed on each fraction, with the following results:

Fraction #	Time (min.)	TNF (pg/ml)
1	5.6-6.25	203
2	6.25-6.6	-157
3	6.6-7.1	1
4	7.1-7.9	11
5	7.9-8.4	84
6	8.4-8.9	-24
7	8.9-9.4	-10
8	9.4-10.0	36
9	10.0-10.4	24
10	10.4-12.0	11
11	12.0-13.6	49
12	13.6-14.2	39
13	14.2-15.35	-9
14	15.35-16.75	39
15	16.75-18.20	-5
Whole VIRULIZIN™		213

Accordingly, the majority of the active components of VIRULIZIN™ eluted in Fraction 1. Activity was also found in Fractions 4-5, 8-9, 11-12, and 14.

Samples from all RP-HPLC fractions were analyzed by mass spectroscopy in accordance with Example 12. A review of the resultant spectra for the fractions indicated that the following compounds were likely present: taurocholic acid, a sialic acid-glycerol dimer, NaCl, trimethylamine, methylethylamine, and propylamine.

Example 16

This example illustrates the compounds that have been identified in the inventive composition.

The inventive composition was prepared in accordance with Example 1 and subjected to standard methods of fractionation, including (1) dialysis in 100 MWCO dialysis membrane; (2) classical organic extractions including Folch extractions, (Tamari et al., Agr. Biol. Chem., 40 (10), 2057-2062 (1976)); (3) silica column chromatography; (4) ion exchange chromatography); and (5) preparative silica TLC fractionation using butanol: acetic acid: water 6:2:2 as the eluant and

ninhydrin as the visualization reagent, using standard methods as disclosed in Dying Reagents for Thin Layer and Paper Chromatography, E. Merck, Darmstadt, Germany, 1971.

Identification of the compounds was based on the following instrumentation and techniques, used individually or in combination:

A VG 70-250S spectrometer was used to obtain EI-MS, CI-MS (OH-,), and FAB-MS (in glycerol or thioglycerol matrices). A VG Analytical Model ZAB-SE instrument was used to obtain EI-MS, FAB-MS (in glycerol or thioglycerol matrices), and GC-MS. The gas chromatograph (GC) used in conjunction with the instrument was a Hewlett Packard model 5890. A Kratos profile spectrometer was used to obtain EI-MS, LSIM-MS (in glycerol and NPOE matrices), and GC-MS mass spectra. The GC used in conjunction with the instrument was also a Hewlett Packard model 5890. MS-MS, electrospray using either water or water alcohol (methanol or isopropyl alcohol) mixtures as solutes, EI-MS and FAB-MS in glycerol and thioglycerol were performed on a perkin-Elmer Sciex API-III spectrometer. Fractions were derivatized for MS analysis as required by acetylation with acetic anhydride/pyridine or methylation with diazomethane. Conversion of molecules into sodiated species was accomplished by addition of sodium acetate to the electrospray solute. Protonation of molecules for electrospray MS was achieved using acetic acid or trifluoroacetic acid. TLCs of extracts and standards were run on silica TLC plates using butanol:acetic acid: water 6:2:2 or cited eluants as mobile phases and several reagent sprays for visualization.

Standard methods were used in connection with the aforementioned instruments, which are further recited in the following references: Rigler et al., J. Chromatography, 277, 321-327 (1983); Sundaram, et al., Clinica Chimica Acta, 34 425-429 (1971); Bandurski et al., J. Biol. Chem., 193 405-410 (1951); and Larsen et al., J. Chromatography, 226 484-487 (1981).

Typical TLC profiles on silica plates (using butanol:acetic acid: water, 6:2:2 as the eluant) are as tabulated for active lots of VIRULIZIN™:

Visualization Reagent	TLC Profile*
sulfuric acid	R*f*=0 to 0.25, white spot
ceric ammonium sulfate	R*f*=0.05 to 0.42, yellow spot

molybdate	Rf=0 to 0.3, pale blue-green to white spots with blue-green edges
anisaldehyde	Rf=0.03 to 0.25, whit spot
8-anilino-1-napthalene sulfonic acid	Rf=0 to 0.25, yellow spots (by eye)
ninhydrin	Rf=0 to 0.13, pale pink spot Rf=0.12 to 0.3, purple spear-headed shaped spot Rf=0.15 to 0.3, burgundy spot Rf=0.3 to 0.45, pale yellow-colored spot Rf=0.35 to 0.5, deep yellow-colored spot Rf=0.4 to 0.5, burgundy spot Rf=0.5 to 0.6, burgundy spot
* Rf values will vary slightly depending on the degree of activity of the silica gel coating of the plates and the precise composition of the elution solvent.	

Analysis of the inventive composition using the aforementioned instrumentation and methods revealed the following compounds contained therein:

1) BILE ACIDS:

cholic acid;

glycocholic acid;

deoxyglycocholic acid;

cholesterol sulfate;

deoxycholic acid;

chenodeoxycholic acid; and

taurocholic acid.

Note: From the MS it is not distinguishable if -OH and $-H_2$ are occurring in the MS or if the deoxy, dideoxy and unsaturated analogs are also present to begin with. These compounds may all be present as salts of ammonium, alkylammonium and inorganic cations.

2) PHOSPHOLIPIDS, SPHINGOLIPIDS AND RELATED (HYDROLYSIS) PRODUCTS:

stearic acid $CH_3(CH_2)_{16}COOH$;

palmitic acid $CH_3(CH_2)_{14}COOH$;

oleic acid Z-9 octadecanoic acid:

$CH_3(CH_2)_2CH_2CH=CHCH_2(CH_2)_6COOH$

oxidized or hydroxylated/unsaturated short chain

fatty acids, such as $C_6H_8O_3$ ($CH_3CH=CH-COCH_2COOH$ or a

C_6 acid with 2 double bonds and a hydroxide);

acetic acid;

stearic acid diglyceride;

palmitic acid diglyceride;

stearic acid, palmitic acid diglyceride;

stearic acid monoglyceride-phosphocholine (a lysolecithin);

stearic acid monoglyceride;

stearic acid triglyceride;

phosphocholine;

phosphoserine;

phosphosphingosine;

sphingomyelin;

lecithin;

stearic acid-sphingosine;

sphingosine;

phosphoglycerol;

glycerol;

choline;

glycero-phosphocholine;

stearic acid, oleic acid diglyceride;

stearic acid, oleic acid phosphoglycerol;

stearic acid amide;

stearic acid methylamide; and

palmitic acid amide.

In addition, preliminary HPLC and titration evidence has been obtained which shows that shorter chain fatty acids are also present (acids range from C_1 to C_{30}).

3) MUCIN HYDROLYSIS PRODUCTS:

sialic acids and their mono and diacetylated monomers;

N-acetylneuraminic acid;

hexosamines, such as glucosamine;

L-fucose;

hexosamine-hexuronic acid (dimer) disulfate;
glucuronic acid;
glucuronic acid or iduronic acid disulfate, monoacetylated;
sialic acid-glycerol (dimer); and
dimers, trimers, oligomers and polymers of the above monomers in acetylated and sulfated form.

4) FAT-SOLUBLE VITAMINS:

Vitamin A2;
Vitamin D1;
lumisterol (present from its vitamin D1 complex);
Vitamin E;
Vitamin K1 oxide; and
Vitamin K5.

5) MISCELLANEOUS ORGANIC:

urea;
alkyl amines, including methyl amine, dimethylamine, ethylamine, methylethylamine, diethylamine, dipropylamine, butylethylamine;
amino acids, including taurine, glutamic acid, glycine, alanine, n-leucine, phosphoserine, phosphoethanolamine, aspartic acid, threonine, serine, sarcosine, α-amino adipic acid, citrulline, valine, isoleucine, β-alanine, γ-amino butyric acid, hydroxylysine, ornithine, and lysine;
butylated hydroxy toluene (BHT); and
polyethylene glycol.

Example 17

This example illustrates the saccharide components of the invention.

The monosaccharide composition of the samples was determined before and after hydrolysis. All reagents used to analyze the monosaccharides were of analytical grade. THF (trifluoroacetic acid) obtained from Aldrich after dilution with deionized water, was used for the hydrolysis of samples. A 50% (W/W) NaOH solution (low in carbonate) was purchased from Fisher Scientific. Sodium acetate was from Fluka-Gerantie, New York.

To release the monosaccharides, the samples were treated with 4M trifluoroacetic acid for 4 hours at 100°C. The samples were lyophilized and analyzed by high performance liquid chromatography-anion exchange using a Dionex Bio-LC System for carbohydrates with Carbopack Pa1 separating column (250 × 4 mm i.d.) and HPLC-AG6 guard column (50 × 4 mm i.d.) equipped with a 25 ul sample loop. Detection of eluting monosaccharides was accomplished with PAD, i.e., pulsed amperometric detector. Conditions were as follows:

Before Hydrolysis

For detection of inositol, sialic acid and glucuronic acid, isocratic elution eluant (100 mM NaOH+150 mM NaOAc mixture) was used. The eluant was protected from the atmosphere with a helium module degasser. The flow rate was 1 ml/min through the column.

Detection of monosaccharides, including fucose, galactosamine, galactose, glucose and mannose, also was accomplished via isocratic elution, eluant (15 mM NaOH) with a post column 300 mM NaOH, at a flow rate 1 ml/min.

The detector settings E1=0.05V, E2=0.60V, E3=0.60 V, t1=120ms, t2=120ms, t3=300ms; gold working electrode; silver-silver chloride reference electrode; output range 1-3 K nAmp full scale; chart speed 0.5 cm/min.

Measurements were performed of the detector for uronic acid and monosaccharides. A linear response was obtained for concentrations varying from 0.5-2.5 ug/ml by a progressive dilution of

a standard mixture.

After Hydrolysis

Monosaccharides were detected after hydrolysis of the sample after applying a gradient elution, eluant A (50 mM NaOH) and eluant B (50 mM NaOH/150 mM NaOAc mixture). The eluants were protected from the atmosphere with a helium module degasser. A Spectra-Physics (SP 4270) integrator was used to analyze the output. The standard gradient was injection in 100% eluant A, followed by a linear progression to 80% A:20% B over the next 10 minutes. This condition was maintained for 20 minutes and then the eluant returned to 100% A over 5 minutes followed by at least 10 minutes of equilibration before injection of the next sample.

The results of the monosaccharide analysis as described are presented in the following table:

Sample / Sugar	MU100 (water layer from a Folch extraction		MU 148 A (dialyzed MU100B)		MU 115 A (dialyzed premix A lot BC0241)		MU100 GB (ethyl acetate extract from green bile)	
	before hydrolysis	after hydrolysis	before hydrolysis	after hydrolysis	before hydrolysis	after hydrolysis	before hydrolysis	after hydrolysis
inositol				same rt of glycerol		same rt of glycerol		same rt of glycerol
sialic acid		<279.3 ng/mg		0		0	3.67 µg/mg	0
glucuronic acid	0	284.4 ng/mg	0	0	0	3.02 µg/mg	4.04 µg/mg	826.58 ng/mg
galacturonic acid								
fucose	0		0		0		0	
galactosamine	0		0		0		0	
glucosamine		<139.6 ng/mg		543.02 ng/mg		234.5 ng/mg		
galactose	0		0		0		0	
glucose	0		0		0		0	
mannose	0		0		0		0	

unknown (most likely glycerol phos-phate		yes			strong peak of unknow n com-pound			

As noted in the table, only the ethyl acetate extract of green bile (batch MU100 GB) was shown to include any monosaccharide prior to hydrolysis, those being sialic and glucuronic acids, in microgram per milliliter concentration. After hydrolysis, no sialic acid was detected and the glucuronic acid was present at approximately 20% the concentration. After hydrolysis, other preparatives of the inventive compositions were shown to contain sialic acid, glucuronic acid, glucosamine, and inositol.

Example 18

This example illustrates the antiviral effects of VIRULIZIN on a patient infected with an HIV virus and demonstrating advanced stage IV-D disease with Kaposi's sarcoma. This patient experienced a reduction in viral load which was associated temporarily with the administration of VIRULIZIN.

This patient was enrolled in Imutec's Corporation Inc., open, non-comparative Phase I/II trial of VIRULIZIN-2y in HIV infected patients with stage IV-D disease (Protocol CO5-107). The objective of this study was to determine the safety, toxicity and effect of VIRULIZIN when administered intramuscularly to HIV patients.

Eligible patients had: (i) documented HIV infection (by confirmatory serologic testing) that meets CDC stage IV-D classification, advanced Kaposi's sarcoma (and lymphoma) recalcitrant to conventional therapy; (ii) ECOG performance status of ≤ 2 or Karnofsky status of $\geq 50\%$ and life-expectancy of at least 12 weeks; (iii) adequate bone marrow and organ function with a haemoglobin count of ≥ 85g/L, neutrophil count of $\geq 1.0 \times 10^9$ / L, and a platelet count of $\geq 75 \times 10^9$ / L, Liver function tests ALT and AST ≤ 5 times above normal values, alkaline phosphate and total bilirubin ≤ 3 times above normal values. Prothrombin time and partial thromboplastin time should not be more that 2 seconds above normal control value. BUN should be normal ($\leq$

10 mmol/L) and serum creatinine ≤ 150 μmol/L).

Baseline clinical evaluations were performed within two weeks prior to patient entry into trial. Evaluations included medical history, physical examination, ECOG/Karnofsky performance status, ECG and chest X-ray. Baseline clinical evaluations also involved laboratory tests including: (i) Hematology; hemoglobin, hematocrit, WBC with differential and platelet coults, prothrombin and partial thromboplastin times. (ii) Blood Chemistry; blood urea nitrogen (BUN), creatinine, uric acid, biliribin, alkaline phosphatase, lactic dehydrogenase (LDH), total protein, albumin, calcium, phosphorus, blood sugar, serum glutamic-oxaloacetic transaminase [SOGT, (AST)], serum glutamate-pyruvate transaminase [SGPT, (ALT)]. (iii) Urinalysis; pH, specific gravity, albumin, glucose, protein, ketones and microscopic (WBC, RBC, casts and bacteria).
Further evaluations involved Quality of Life Assessment, symptom assessment, immune status assessment, delayed hypersensitivity skin test (modified Sokal method) tumor measurements, photography of lesions and recording of previous and concomitant medications. The patient was followed until death to generate survival analysis data.

The patient was male, 33 years of age, fulfilled the inclusion criteria for enrolment into the clinical trial, and was diagnosed as having Kaposi's sarcoma.

During the course of treatment, the patient received 15 intramuscular injections with VIRULIZIN over a 3 week period. On day 5 of this clinical study, this patient also began to receive 150mg BID of Lamivudine (3TC). In addition, starting on day 14, 800mg TID of Indinavir (Ceixivan) was also provided.

Viral Load (Plasma Branch DNA)

Baseline	70,690 copies/mL	Day 0
Week 2	727 copies/mL	Day 14
Week 3	500 copies/mL	Day 22

CD4 Counts

Baseline	CD4%	2	Abs	38	Day 0

Week 2	CD4%	1	Abs	13	Day 14
Week 3	CD4%	2	Abs	38	Day 22

Example 19

This example illustrates the activation of monocytes and macrophages with the composition of Example 1 and methods for testing same.

Investigations have shown that the composition of Example 1 will activate normal monocytes to demonstrate cytotoxicity towards the Chang hepatoma cell line, which is used to measure monocyte toxicity, and that the monocytes and macrophages from cancer patients (e.g., those afflicted with cancers of the cervix, ovaries, ear/nose/throat, and endometrium/uterus, and chronic myelogenous leukemia) have been stimulated by the composition to attack and destroy tumor cells derived from the same patient.

More particularly, the monocyte tumoricidal function has been tested in the presence of the composition of the invention and the basic procedure for these experiments is outlined below. This procedure has been named the "Monocyte/Macrophage Cytotoxicity Assay to Cell Lines and Autologous Tumor Cells," or "Cytotoxicity Assay" for short.

The method requires isolation of monocytes/macrophages, which is accomplished as follows: Venous blood is collected aseptically in heparinized Vacutainer tubes. Sterile preservative-free heparin is added to a final concentration of 20 units/ml. The blood is diluted 3:1 in Hanks balanced salt solution (HBSS), layered onto lymphocyte separation medium and centrifuged to obtain a band of peripheral blood mononuclear cells (PBMNs). After centrifugation, the mononuclear cell layer is recovered from the interface, washed twice in medium (medium is Roswell Park Memorial Institute [RPMI] 1640 media supplemented with 10% heat-inactivated fetal bovine serum, 50 units/ml penicillin, and 50 μg/ml streptomycin) and monocytes are enumerated by latex ingestion. Monocytes are isolated by adherence in 96-well plastic plates (for 2 hours at 37° C, followed by two cycles of washing with medium). Adherent cells are estimated to be greater than 90% monocytes. Wells containing adherent cells are incubated overnight in the presence of VIRULIZIN™ (1:10-1:200 final dilution). Then, adherent cells

are washed to remove VIRULIZIN™ and incubated overnight with tumor cells. The tumor cells are maintained in medium in which endotoxin concentration is guaranteed by the manufacturer to be low and is non-stimulatory in the assay.

For studies using a standard cell line, ^{51}Cr (chromium) labelled Chang hepatoma cells are used because this cell line is insensitive to natural killer cell cytotoxicity. These hepatoma target tumor cells are added to adherent cell monolayers at effector:target (E:T) cell ratios of 20:1 to 15:1. This E:T ratio is used because it falls well into the plateau range on a curve prepared by varying the E:T ratio from 5:1 to 30:1. After 24 hours, supernatants are collected and ^{51}Cr release is quantitated. The percent specific cytotoxicity is calculated as:

$$\% \text{ specific release} = \frac{E - S}{T - S} \times 100$$

In the equation above, E = CPM released from target cells in the presence of effector cells; S = CPM released from target cells in the absence of effector cells; T = CPM released from target cells after treatment with 2% sodium dodecyl sulfate).

For studies using autologous tumor cells, these cells are obtained from surgical biopsies, labelled with ^{51}C, and used in the same way as the hepatoma cells described above.

Preparation of peritoneal and alveolar macrophages is done by the methods described in Braun et al., Cancer Research, 53, 3362-3365 (1993).

Using this protocol, the composition was found to cause monocytes from healthy donors to exert cytotoxicity toward the Chang hepatoma cell line. Subsequently, whether monocytes and macrophages from a cancer patient could be stimulated by the composition to attack and destroy their own particular tumor was investigated. Using similar protocols as described for the standard cell line (Chang hepatoma cells), monocytes and/or peritoneal macrophages from cancer patients were isolated. Peritoneal macrophages were isolated from peritoneal fluids collected at the time of laparoscopy. The composition was found to activate peripheral monocytes and peritoneal macrophages from a patient with cervical cancer to produce cytotoxicity against the patient's own tumor cells. This effect was comparable to or better than that produced by the combination of IFN and LPS. Peritoneal macrophages from a patient

with ovarian cancer were also found to be stimulated by the composition to attack and destroy the ovarian tumor cells in culture.

Monocyte/Macrophage Studies with the Composition

Because the screening procedures demonstrated that the composition does not stimulate lymphocyte functions but can stimulate monocyte functions, subsequent studies were aimed at further characterization of the monocyte/macrophage stimulatory activities of the composition. A number of comparative studies aimed at determining the dose response characteristics of the composition in stimulating monocyte/macrophage tumoricidal function were performed as well as testing different batches of the compound. The main emphasis of the studies was to test the capacity of the composition to simulate tumoricidal function in monocytes and macrophages from different anatomical sites of cancer patients. For these investigations, the following were relied upon: (1) peripheral blood monocytes from cancer patients and control subjects; (2) alveolar macrophages from lung cancer patients and control patients with non-malignant lung diseases; and (3) peritoneal macrophages from patients with gynecological malignancies.

Dose response studies with different batches of the composition, all prepared in accordance with Example 1, were completed. These studies relied on peripheral blood monocytes to test the stimulatory activities of different doses and different batches of the composition (Batch nos. 216, 219 and 222). Each batch of the composition was tested without dilution (neat), a 1:10 dilution and a 1:50 dilution of material. The results are depicted graphically in Figure 14.

Batch #222 and #216 were shown to stimulate monocyte tumoricidal function, however, Batch #219 did not. It appeared that #222 was superior to #216 in these preliminary investigations. Batch #222 appeared to stimulate equivalent levels of tumoricidal function at the undiluted (neat) and 1:10 dilutions, but lesser, still detectable activity at the 1:50 dilution. Batch #216 gave the greatest stimulation of tumoricidal function at the undiluted (neat) concentration, with less activity at the 1:10 dilution and no detectable activity at the 1:50 dilution. As stated above, Batch #219 did not elicit detectable monocyte tumoricidal function at any concentration tested.

Tumoricidal function in peripheral blood monocytes was also evaluated. Tests were performed on 4 peripheral blood monocyte samples from control subjects. These tests utilized an optimal stimulating concentration of the composition (1:10 dilution of batch #222) and an optimal stimulating concentration of IFN-γ plus LPS. The target cells in these studies were a cultured, NK-insensitive cell line, namely the Chang Hepatoma. Results are presented in the following table.

Stimulant (E/T-20/1)	% Cytotoxicity
Medium	5.4 ± 1
IFN-γ + LPS	18.6 ± 4
Composition	22.3 ± 6

A test was also performed on 1 monocyte sample from a patient with cervical cancer. This test was important because the patient's own tumor cells were available to be used as target cells in the assay. As before, this test utilized an optimal stimulating concentration of the composition (1:10 dilution of Batch #222) and an optimal stimulating concentration of IFN-γ plus LPS. Also, the effector/target cell ratio was reduced to 15/1 to conserve patient tumor cells. Results of this test are presented in the following table.

Stimulant (E/T-20/1)	% Cytotoxicity
Medium	5.5
IFN-γ + LPS	14.4
Composition	20.9

In the peripheral blood monocytes from control subjects, the composition stimulated monocyte tumoricidal function against the Chang Hepatoma cells at a level equal to or greater than the level elicited by an optimal stimulating concentration of IFN-γ + LPS. In the peripheral blood monocytes from a patient with cervical cancer, the composition stimulated tumoricidal function against the patient's own tumor cells at a level which exceeded that elicited by IFN-γ plus LPS by greater than 30%.

Tumoricidal function in peritoneal macrophages from patients with gynecological malignancies was tested. These tests were performed on peritoneal macrophage samples isolated from lavage

fluids of 1 patient with cervical cancer and 1 patient with ovarian cancer. These tests were performed with the patient's own tumor cells as target cells in the assay. As before, an optimal stimulating concentration of the composition (1:10 dilution of Batch #222) and an optimal stimulating concentration of IFN-γ plus LPS were compared. Also, the effector/target cell ratio was reduced to 15/1 to conserve patient tumor cells. The resulting data were:

Stimulant	Cervical Cancer	Ovarian Cancer
Medium	8.2	0.6
IFN + LPS	29.8	4.1
Composition	13.2	8.9

These test results highlighted the fact that the local tumor environment may be a determinant of the response of immune cells to immunological activators. In this case of cervical cancer, there was no pathological evidence of malignant disease within the peritoneal cavity and the development of tumoricidal function against the autologous tumor was better with IFN-γ and LPS combined than with the composition. In the patient with ovarian cancer, there was a significant tumor in the peritoneal cavity. The response against the patient's own tumor to IFN-γ and LPS combined was minimal at best, whereas the response to the composition was greater.

Tumoricidal function in alveolar macrophages from lung cancer patients and control subjects was tested. These tests were performed on alveolar macrophage samples isolated from bronchoalveolar lavage fluids of a patient with non-small cell lung cancer and three (3) patients with non-malignant diseases of the lung. These tests utilized an optimal stimulating concentration of the composition (1:10 dilution of batch #222) and an optimal stimulating concentration of IFN-γ and LPS combined. The target cells in these studies were the Chang Hepatoma cells and the effector/target cell ratio was 20/1. The resulting data were:

Stimulant	Cancer Patients	Control
Medium	2.6 ± 2	19.5 ± 4
IFN-γ+LPS	10.9 ± 13	1.2 ± 5
Composition	5.2 ± 2	18.6 ± 8

The results were consistent with the observation that alveolar macrophages from lung cancer pa-

tients are impaired in their development of tumoricidal function in response to conventional macrophage activators such as IFN-γ + LPS. The results showed that the tumoricidal function of alveolar macrophages from lung cancer patients is greatly reduced compared to control subjects. The data presented earlier indicated VIRULIZIN™ to be a poor stimulator of alveolar macrophages. Further investigation with alveolar macrophages from non-small cell lung cancer patients is presented in Example 23. The activity in alveolar macrophages appears to vary with the VIRULIZIN™ preparation. Thus, alveolar macrophage cytotoxicity was elicited in only 2/7 alveolar macrophage preparations with the origin batches tested (222, 219, 216). In contrast, 3/4 alveolar preparations were stimulated with the later preparations (233, 238). The difference could be related to age and potency of the preparation or patient variability. Accordingly, the composition can activate tumoricidal activity in alveolar macrophages.

The preliminary *in vitro* tests with the composition demonstrate that it is a macrophage activator. The material provided was able to elicit tumoricidal activity in a standard cytotoxicity assay against both an NK insensitive cell line and against freshly dissociated human tumor cells. The activity elicited was also found to be concentration-dependent in these tests. The capacity of the composition to active macrophage tumoricidal function *in vitro* was comparable to that of the best macrophage activating combination presently available, namely, IFN-γ and endotoxin (i.e., LPS) combined. As stated above, the capacity of the composition to elicit this level of tumoricidal function in the absence of endotoxin would be considered important biologically if the material is free of endotoxin contamination. The composition is free of endotoxin contamination when tested for pyrogens by the United States Pharmacoepeia (USP) rabbit pyrogen test.

As has been found for other macrophage activators, the activity of the composition in stimulating macrophage tumoricidal function varies with the source of the macrophages. It appears that the composition is an excellent activator of peripheral blood monocytes being equivalent to IFN-γ + LPS with normal donors and possibly superior to IFN-γ + LPS with cancer patient donors. Malignant disease has a significant impact on the development of monocyte tumoricidal function depending on the activator used (Braun et al., (1991)). One determinant of the biological activity of different macrophage activators in cancer patients monocytes is the sensitivity of the activator to arachidonic acid metabolism and the secretion by the cell of prostaglandins. From these initial studies with the composition, it appears that activity elicited with the compound is not sensitive to the inhibitory effects of prostaglandins. If prostaglandin insensitivity can be proven definitively

for cancer patient monocytes stimulated with the composition, this would be considered important therapeutically because the effectiveness of many other biological activators is limited by prostaglandins. Preliminary studies with 2 specimens indicate that the composition may have good activity in peritoneal macrophages, particularly when malignant disease is present in the peritoneal cavity.

These preliminary results also illustrate what has been found when comparing the capacity of different activators to stimulate tumoricidal function in peritoneal macrophages of patients with different gynecological malignancies. In those studies, it was found that the presence of malignant disease within the peritoneal cavity influences the responsiveness of the peritoneal macrophages to specific activators. In patients with cervical cancer, malignant disease is not present in the peritoneal cavity in general, and thus, the response of the resident macrophages to IFN-γ + LPS is normal. When disease is present in the cavity, however, as in the case with ovarian cancer, the response to lFN-γ + LPS is suppressed. This is related, in part, to changes in the arachidonic acid metabolism of the peritoneal macrophages when malignant disease is present (Braun et al., 1993). The fact that the composition activates tumoricidal function in peritoneal macrophages from ovarian cancer patients against the patient's own tumor cells is consistent with a mechanism for activation that is independent of the arachidonic acid metabolic pathway.

Accordingly, as shown in the aforestated *in vitro* studies, the composition of the present invention is able to activate monocytes and macrophages to increase their immune system function.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. An antiviral cocktail comprising:

(i) a composition comprising small molecular weight components of less than 3000 daltons, and having the following properties:

a) is extractable from bile of animals;

b) is capable of stimulating monocytes and macrophages in vitro;

c) is capable of modulating tumor necrosis factor production;

d) contains no measurable level of IL-1a, IL-1b, TNF, IL-6, IL-8, IL-4, GM-CSF or IFN-gamma;

e) shows no cytotoxicity to human peripheral blood mononuclear cells;

f) is not an endotoxin; and

(ii) an effective amount of one or more antiviral agent(s).

2. The antiviral cocktail of claim 1, as characterized wherein the composition or antiviral agent(s) have a specific activity greater than that of the composition or antiviral agent(s) alone.

3. The antiviral cocktail of claim 1, wherein said antiviral agent(s) are selected from the group comprising 3TC, interferon, ganciclovir, famciclovir, rimantadine, foscarnet sodium, zidovudine, amantadine hydrochloride, valacyclovir, ribavirin and acyclovir.

4. A method for diminishing the viral load in a host infected with a virus, comprising the administration of the antiviral cocktail of claim 1.

5. An antiviral pharmaceutical composition comprising, as an active ingredient, an effective antiviral amount of the cocktail of claim 1 and a non-toxic pharmaceutically acceptable carrier of diluent.

6. The antiviral pharmaceutical composition of claim 5, formulated into a sterile solution, a lyophilate, pills, tablets, creams, gelatin capsules, capsules, suppositories, soft gelatin capsules, gels, membranes, and tubelets.

7. The use of the antiviral pharmaceutical composition of claim 5, to diminish the viral load in a host infected with a virus, comprising the administration of said pharmaceutical composition by means of oral, topical, rectal, parenteral, local, inhalant, or intracerebral delivery.

8. The use according to claim 7, wherein said parenteral delivery is achieved via intramuscular injection.

9. The use according to claim 7, wherein said virus is a retrovirus.

10. The use according to claim 9, wherein said retrovirus is human immunodeficiency virus.

11. The use according to claim 7, wherein said host is human.

12. A method for diminishing the viral load in a host infected with a virus, comprising the administration of an antiviral effective amount of a composition comprising small molecular weight components of less than 3000 daltons, and having the following properties:

a) is extractable from bile of animals;

b) is capable of stimulating monocytes and macrophages in vitro;

c) is capable of modulating tumor necrosis factor production;

d) contains no measurable level of IL-1a, IL-1b, TNF, IL-6, IL-8, IL-4, GM-CSF or IFN-gamma;

e) shows no cytotoxicity to human peripheral blood mononuclear cells; and

f) is not an endotoxin.

13. The method of claim 12, wherein said antiviral effective amount of the composition additionally comprises a non-toxic pharmaceutically acceptable carrier of diluent.

14. The method of claim 12, wherein said composition is formulated into a sterile solution, a lyophilate, pills, tablets, creams, gelatin capsules, capsules, suppositories, soft gelatin capsules, gels, membranes, and tubelets

15. The method of claim 12, said administration is achieved by means of oral, topical, rectal, parenteral, local, inhalant, or intracerebral delivery.

16. The method of claim 12, wherein said parenteral administration is achieved via intramuscular injection.

17. The method of claim 12, wherein said virus is a retrovirus.

18. The method of claim 17, wherein said retrovirus is human immunodeficiency virus.

19. The method of claim 12, wherein said host is human.

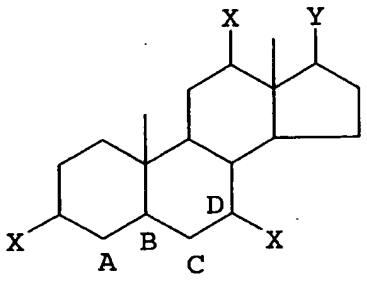
20. The method of claim 12, wherein the viral load is diminished by stimulating peripheral blood monocytes and/or tumor associated macrophages to express cytocidal activity in a manner that is insensitive to the inhibitory effects of prostaglandins.

21. The method of claim 12, wherein the viral load is diminished by eliciting suitable modulation of the immune system in a patient in need of such modulation by activating macrophages and/or monocytes to produce cytokines or promote activity to seek and remove or destroy disease-causing viruses or cells negatively affected by such viral infections.

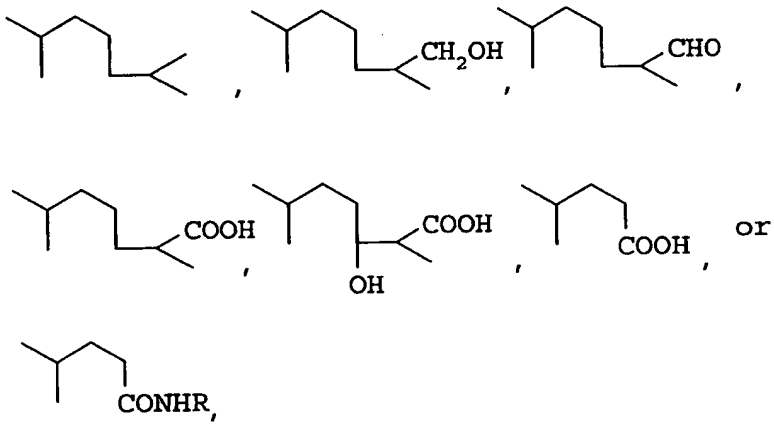
22. The method of claim 12, wherein the viral load is diminished by stimulating the release of TNF, Il-1β and GM-CSF.

23. A use of a composition to diminish the viral load in a host infected with a virus, comprising administering an effective amount of said composition, extracted from bile, comprising at least one of the following compounds:

(a) a compound of the formula

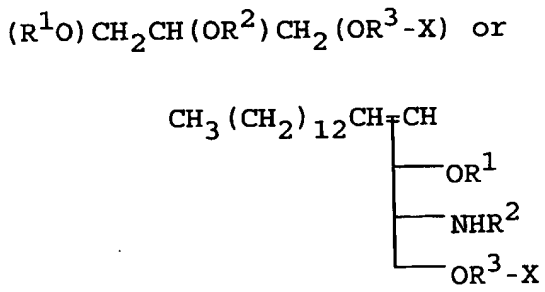


where the bonds between A-B, B-C, and C-D may be single or double bonds, and where x=H, OH, =O, or OSO_3H; and Y=



where R is an amino acid residue;

(b) a compound of the formula



where R^1, R^2 and R^3 are H, COR^4, CH=CH-R^5, X, P(O)(OH)O-, or -$S(O)_2O$-;

X is choline, ethanolamine, N-alkylated ethanolamines, serine, inositol, sugars bearing free hydroxyls, amino-sugars, sulfonated sugars, or sialic acids; and

R^4 is a saturated or unsaturated alkyl group having a carbon chain from about C_1 to C_{30}, or oxidized and hydroxylated analogs thereof; and

R^5 is an alkyl group or oxidized and hydroxylated analogs thereof;

(c) a mucin hydrolysis product or a proteoglycan hydrolysis product; or

(d) a fat-soluble vitamin, with the proviso that retinol and retinol derivatives are not included.

24. The use according to claim 23, wherein said composition comprises at least one compound selected from the group consisting of taurocholic acid and its sulphated derivatives; glycocholic acid and its sulphated derivatives; sphingosine; a diacyl glycerol; phosphocholine; glucosamine-3-sulfate; glycero-phosphocholine; phosphoryl choline chloride; lecithin; an oligosaccharide of less than 10 saccharide units in length, where said oligosaccharide is comprised of sialic acid, fucose, hexosamines, or sulphated hexosamines; taurine; and glutamic acid and its conjugates.

25. The use according to claim 23, wherein said composition additionally comprises at least one compound selected from the group consisting of ammonia; primary alkyl amines; secondary alkyl amines; tertiary alkyl amines; and a carboxylic acid R^6CO_2H, wherein R^6 is C_1-C_{30} alkyl, saturated or unsaturated, and oxidized or hydroxylized derivatives thereof.

26. The use according to claim 23, wherein said composition comprises at least one compound selected from the group consisting of taurocholic acid and its sulphated derivatives; glycocholic acid and its sulphated derivatives; sphingosine; a diacyl glycerol; phosphocholine; glucosamine-3-sulfate; glycero-phosphocholine; phosphoryl choline chloride; lecithin; an oligosaccharide of less than 10 saccharide units in length, where said oligosaccharide is comprised of sialic acid, fucose, hexosamines, or sulphated hexosamines; Vitamin A; retinolic acid derivatives; taurine; and glutamic acid and its conjugates.

27. The use according to claim 23, wherein said virus is a retrovirus.

28. The use according to claim 27, wherein said retrovirus is human immunodeficiency virus.

29. The use according to claim 23, wherein said host is a human.

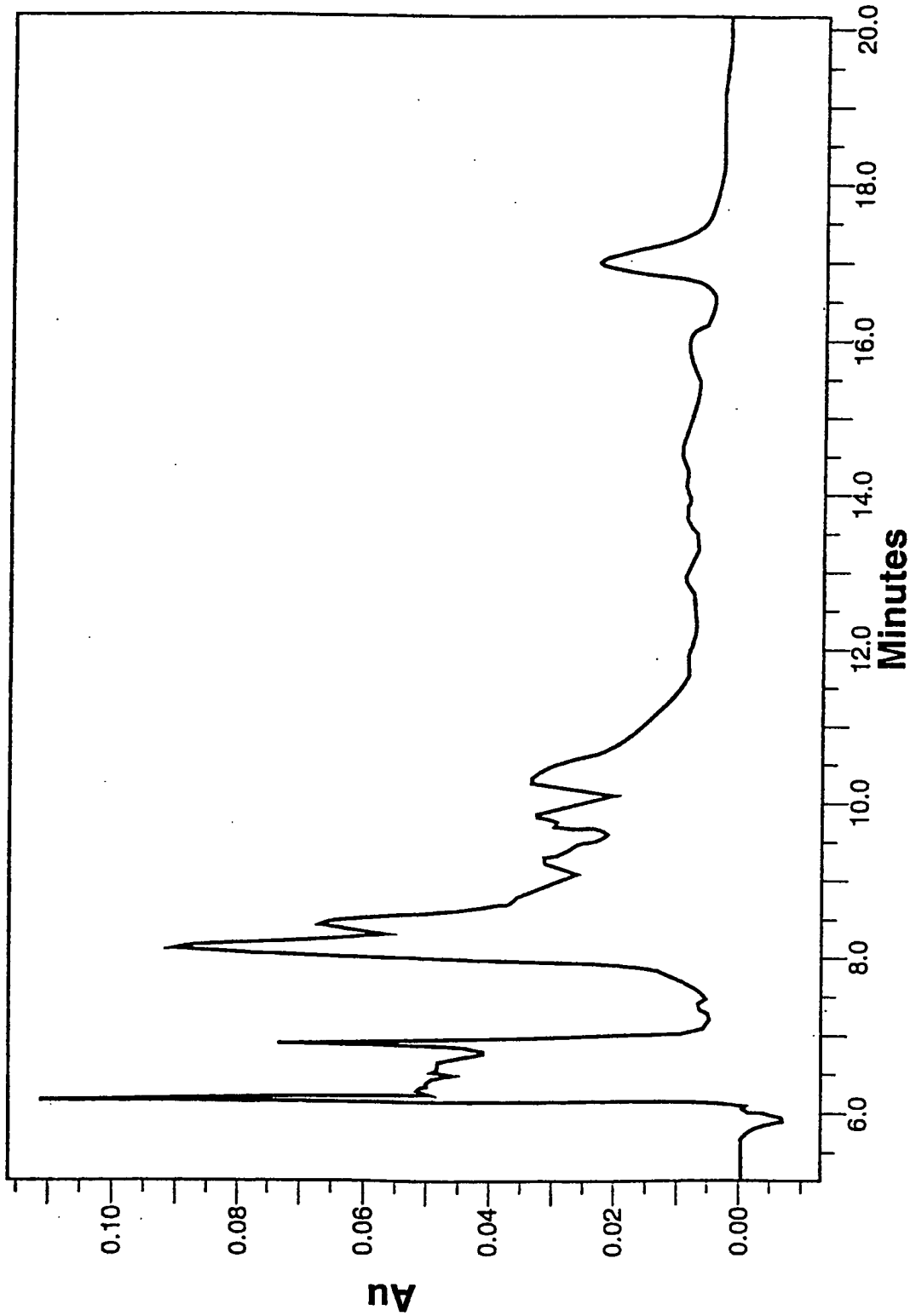


FIG. 1

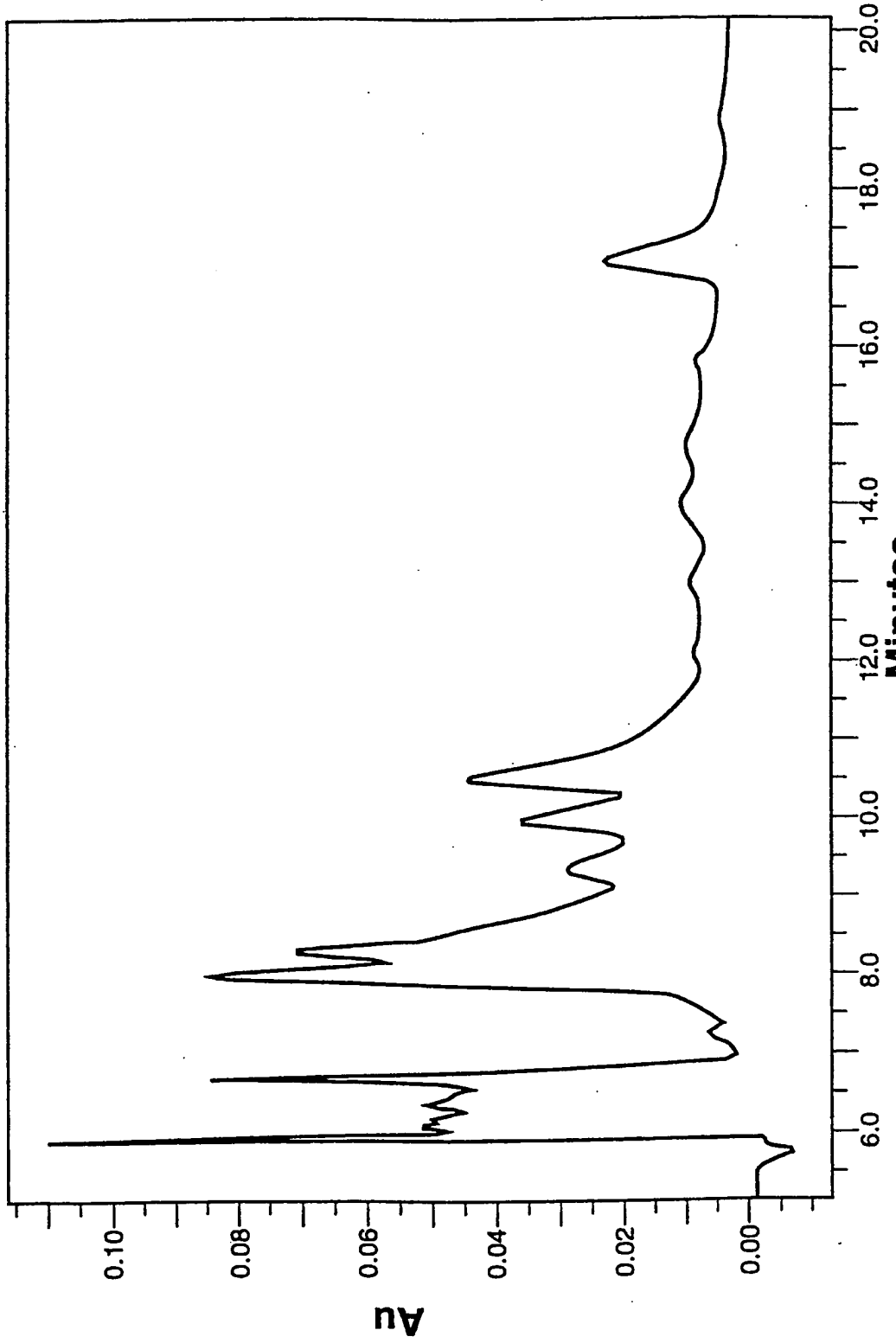


FIG. 2

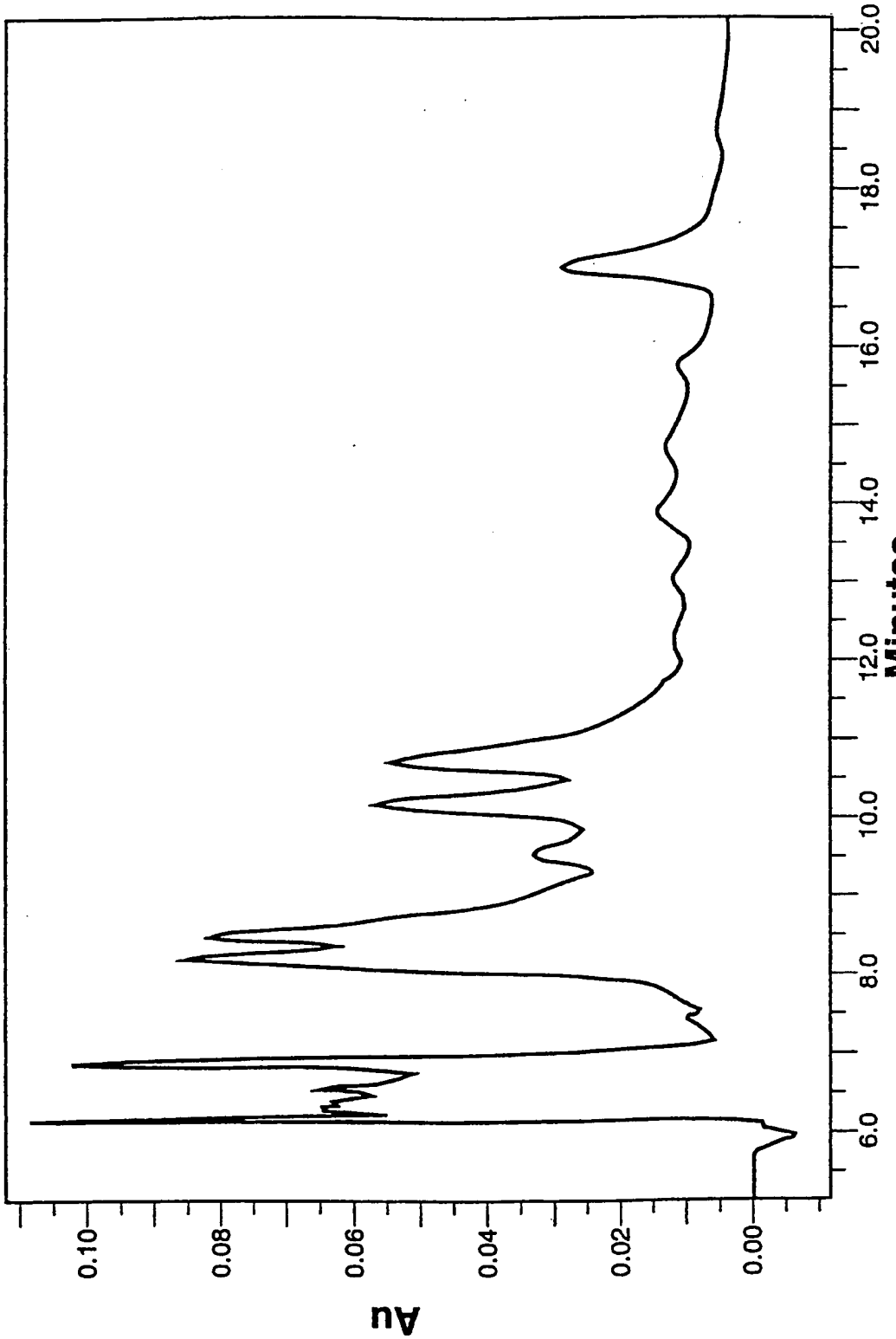


FIG. 3

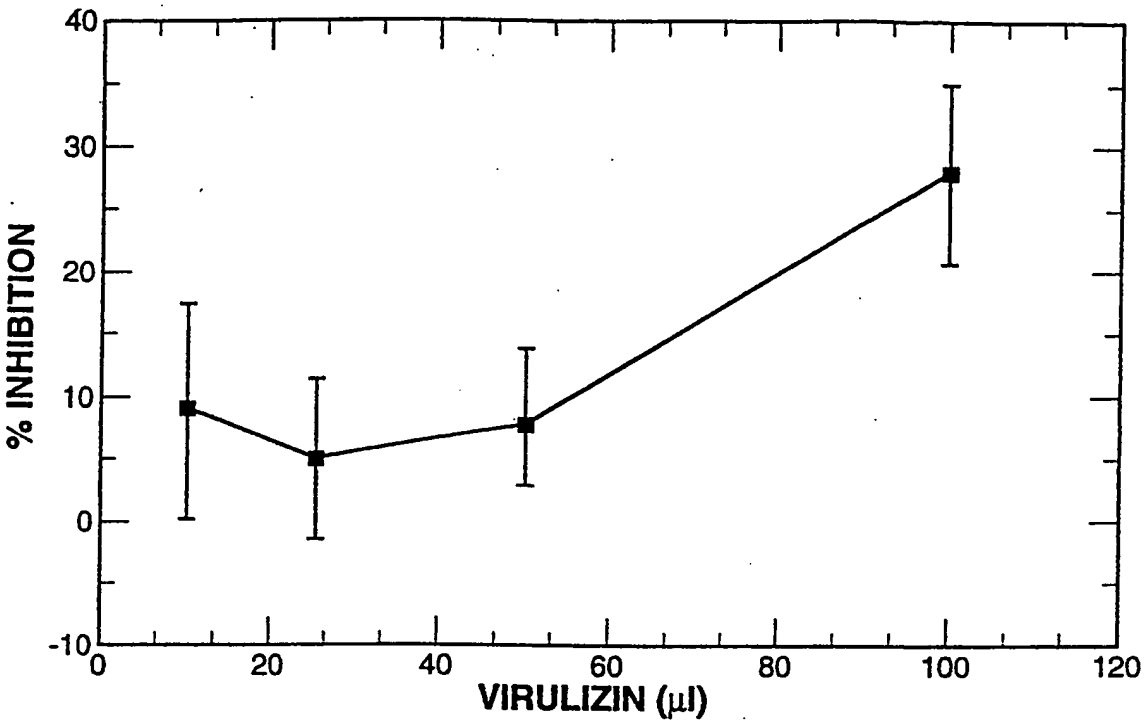

40
30
20
10
0
-10
% INHIBITION
0
20
40
60
80
100
120
VIRULIZIN (µl)

FIG. 4

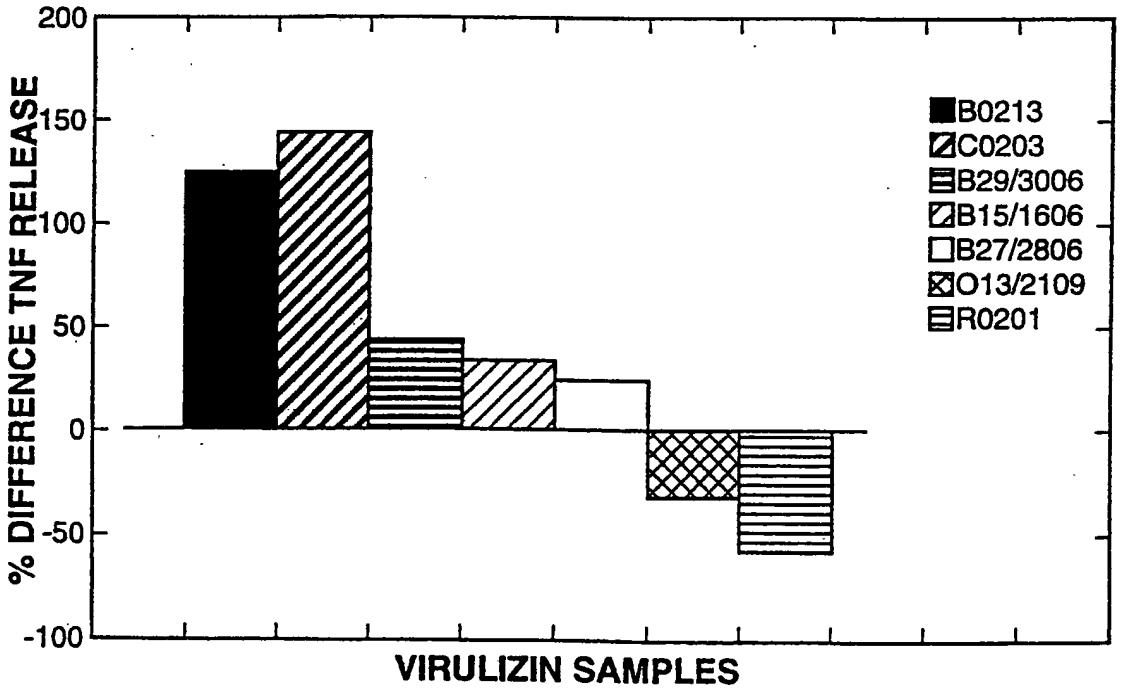

200
150
100
50
0
-50
-100
% DIFFERENCE TNF RELEASE
B0213
C0203
B29/3006
B15/1606
B27/2806
O13/2109
R0201
VIRULIZIN SAMPLES

FIG. 5

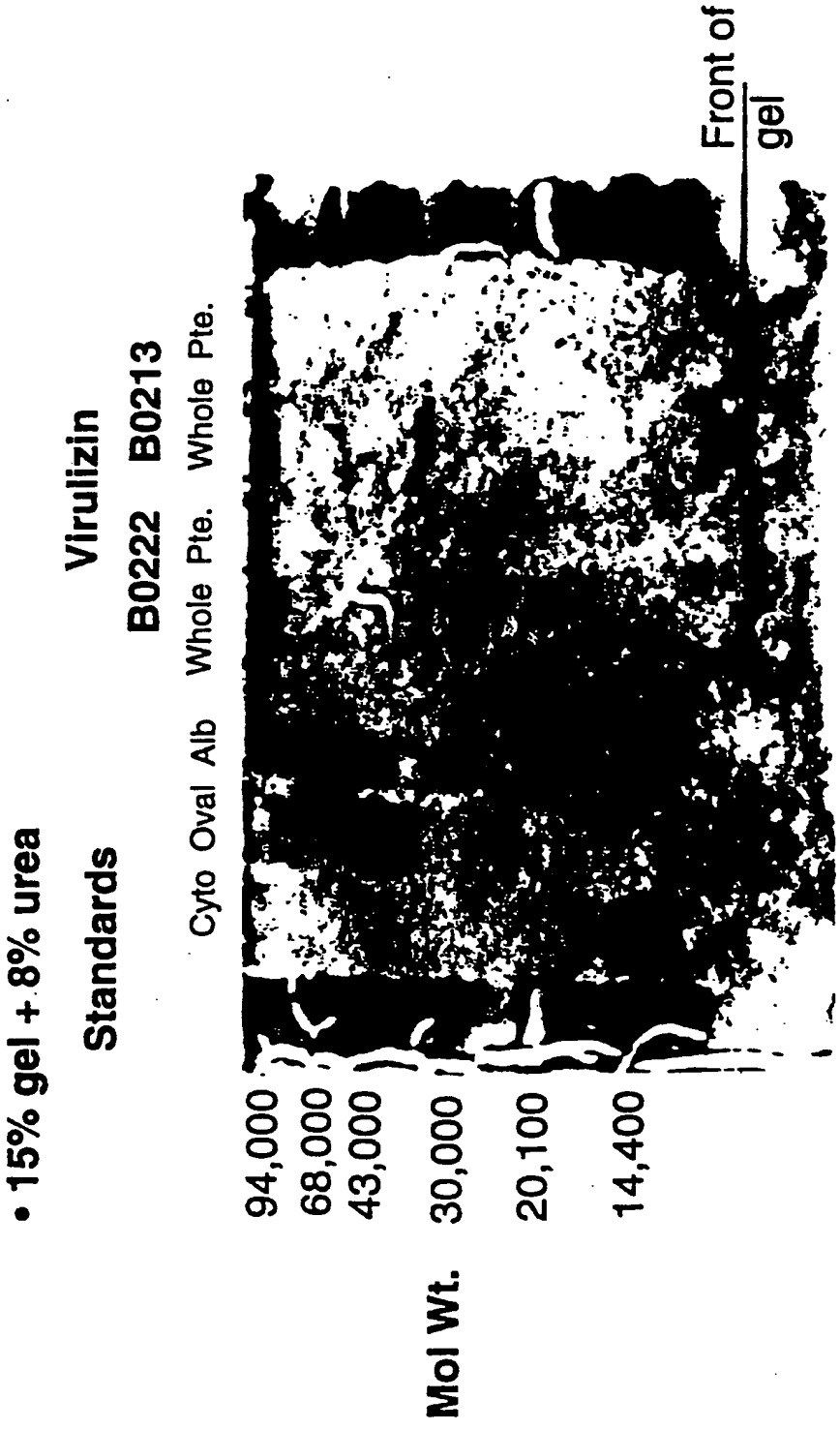

• 15% gel + 8% urea
Standards
Virulizin
B0222 B0213
Cyto Oval Alb Whole Pte. Whole Pte.
Front of gel
94,000
68,000
43,000
30,000
20,100
14,400
Mol Wt.

FIG. 6

HYDROPHILIC COLUMN

Date: 14 Sept. 1993

COLUMN: HYDROXYETHYL
BUFFER: 50mM Formic
FLOW RATE: 1ml/min
O.D.: 254 nm
CHART SPEED: 0.5 cm/min

Time (min)	Substance	Peak Height (inch)
	Virulizin B0213	
6.32	whole	8.00
8.22		2.60
9.07		10.00
10.30		0.70
13.25		0.90
6.58	supernatant	10.00
8.29		1.00
10.00		0.55
13.40		0.60
6.38	precipitate	3.50
8.23		0.25

FIG. 7A

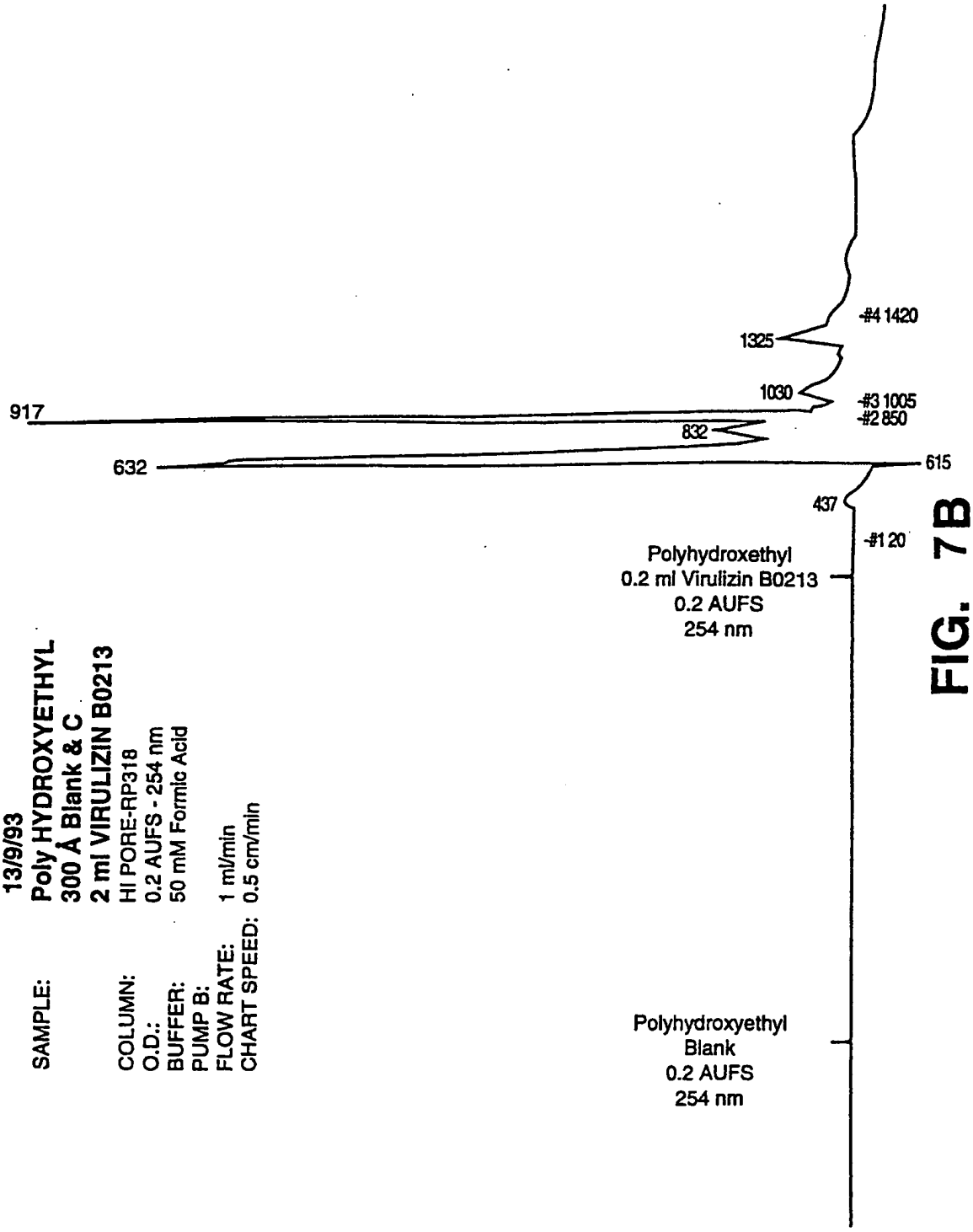

#4 1420
1325
1030
#3 1005
#2 850
917
832
632
615
437
#1 20
Polyhydroxethyl
0.2 ml Virulizin B0213
0.2 AUFS
254 nm
Polyhydroxyethyl
Blank
0.2 AUFS
254 nm
SAMPLE: 13/9/93 Poly HYDROXYETHYL 300 Å Blank & C 2 ml VIRULIZIN B0213
COLUMN: HI PORE-RP318
O.D.: 0.2 AUFS - 254 nm
BUFFER: 50 mM Formic Acid
PUMP B:
FLOW RATE: 1 ml/min
CHART SPEED: 0.5 cm/min

FIG. 7B

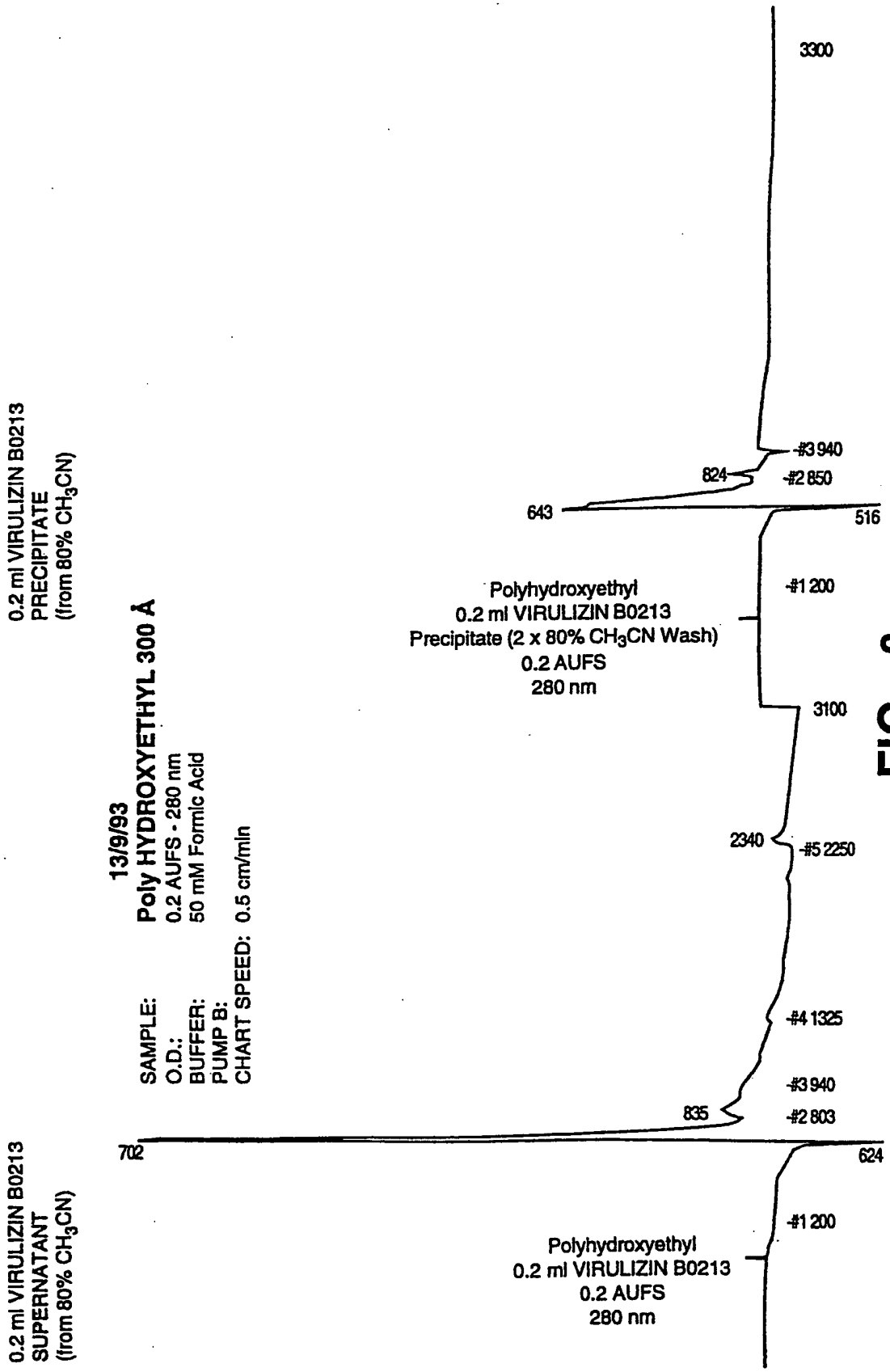

0.2 ml VIRULIZIN B0213
PRECIPITATE
(from 80% CH_3CN)
13/9/93
Poly HYDROXYETHYL 300 Å
SAMPLE:
O.D.:
BUFFER:
PUMP B:
CHART SPEED: 0.5 cm/min
0.2 AUFS - 280 nm
50 mM Formic Acid
3300
#3 940
824
#2 850
643
516
Polyhydroxyethyl
0.2 ml VIRULIZIN B0213
Precipitate (2 x 80% CH_3CN Wash)
0.2 AUFS
280 nm
#1 200
3100
2340
#5 2250
#4 1325
#3 940
835
#2 803
702
624
#1 200
Polyhydroxyethyl
0.2 ml VIRULIZIN B0213
0.2 AUFS
280 nm
0.2 ml VIRULIZIN B0213
SUPERNATANT
(from 80% CH_3CN)

FIG. 8

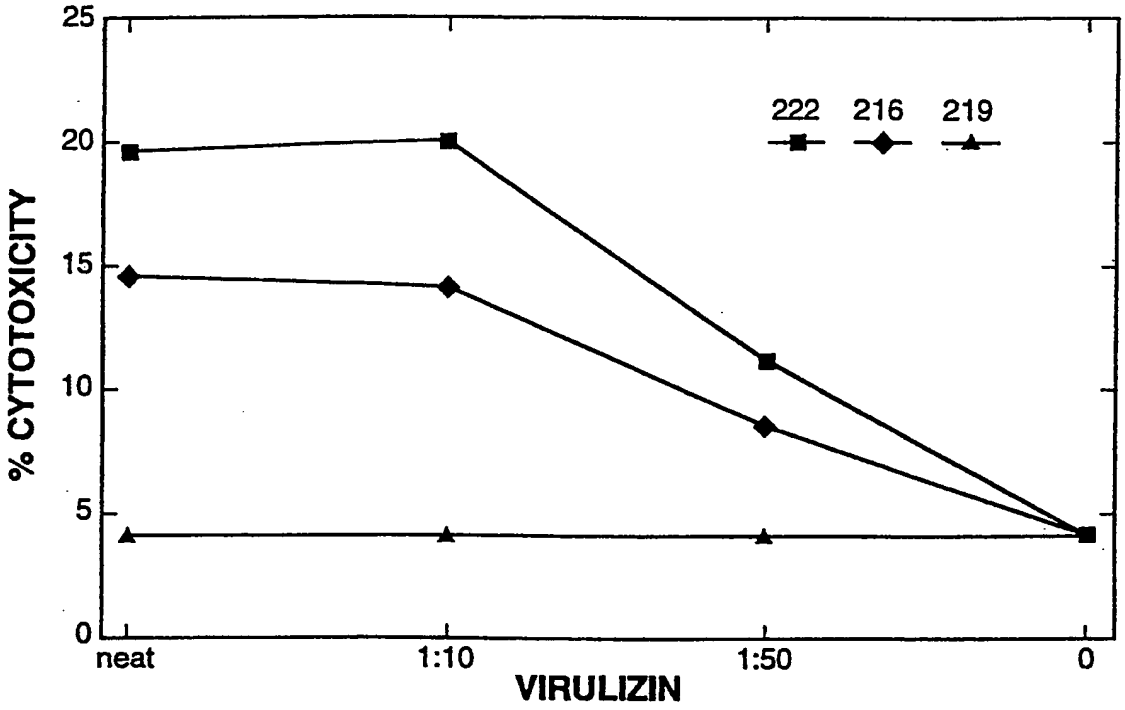

25
20
15
10
5
0
% CYTOTOXICITY
222
216
219
neat
1:10
1:50
0
VIRULIZIN

FIG. 9

~~09/875,150~~ 10/072,128

=> d ibib ab hitstr 1-4

L12 ANSWER 1 OF 4 USPATFULL
ACCESSION NUMBER: 2002:221381 USPATFULL
TITLE: Novel ecdysone receptor-based inducible gene expression system
INVENTOR(S): Palli, Subba Reddy, Lansdale, PA, UNITED STATES
Kapitskaya, Marianna Zinovjevna, North Wales, PA, UNITED STATES
Cress, Dean Ervin, Souderton, PA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002119521	A1	20020829
APPLICATION INFO.:	US 2001-965703	A1	20010926 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2001-US9050, filed on 21 Mar 2001, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-191355P	20000322 (60)
	US 2001-269799P	20010220 (60)

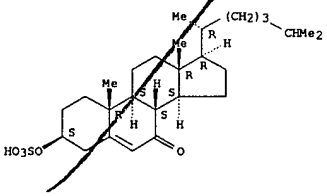
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROHM AND HAAS COMPANY, PATENT DEPARTMENT, 100 INDEPENDENCE MALL WEST, PHILADELPHIA, PA, 19106-2399
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 6231
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the field of biotechnology or genetic engineering. Specifically, this invention relates to the field of gene expression. More specifically, this invention relates to a novel inducible gene expression system and methods of modulating gene expression in a host cell for applications such as gene therapy, large scale production of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic plants and animals.

IT **53216-02-7**, 7-Ketocholesterol-3-sulfate
(regulation of gene expression by; ecdysone receptor fusion proteins and their use in regulation of gene expression)

RN 53216-02-7 USPATFULL
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 1 OF 4 USPATFULL (Continued)

L12 ANSWER 2 OF 4 USPATFULL
ACCESSION NUMBER: 2002:199124 USPATFULL
TITLE: Steriodal derivatives
INVENTOR(S): Liao, Shutsung, Chicago, IL, UNITED STATES
Song, Ching, Chicago, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002107233	A1	20020808
APPLICATION INFO.:	US 2002-72128	A1	20020208 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-267493P	20010208 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Y. ROCKY TSAO, Fish & Richardson P.C., 225 Franklin Street, Boston, MA, 02110-2804
NUMBER OF CLAIMS: 62
EXEMPLARY CLAIM: 1
LINE COUNT: 611
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A compound of formula (1): ##STR1##

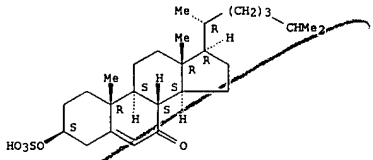
wherein each of R.sub.1, R.sub.2, R.sub.4, R.sub.4', R.sub.7, R.sub.11, R.sub.12, R.sub.15, R.sub.16, R.sub.17, and R.sub.17', independently, is hydrogen, hydroxy, amino, carboxyl, oxo, halo, sulfonic acid, --O-sulfonic acid, or alkyl that is optionally inserted with --NH--, --N(alkyl)-, --O--, --S--, --SO--, --SO.sub.2--, --O--SO.sub.2--, --SO.sub.2--O--, --SO.sub.3--O--, --CO--, --CO--O--, --O--CO--, --CO--NH--, --CO--N(alkyl)-, --NH--CO--, or --N(alkyl)-CO--, and further optionally substituted with hydroxy, halo, amino, carboxyl, sulfonic acid, or --O-sulfonic acid; R.sub.3 is X-Y--, wherein X is hydrogen, amino, carboxyl, halo, sulfonic acid, --O-sulfonic acid, or alkyl; Y is --S--, --NH--, --N(alkyl)-, --SO--, --SO.sub.2--, --O--SO.sub.2--, --SO.sub.2--O--, --SO.sub.3--O--, --CO--, --CO--O--, --O--CO--, --CO--NH--, --CO--N(alkyl)-, --NH--CO--, or --N(alkyl)-CO--; R.sub.5 and R.sub.6, together, are --O--; or R.sub.5 and R.sub.6, together, are a double bond between C-5 and C-6, and R.sub.7 is oxo; each of R.sub.8, R.sub.9, R.sub.10, R.sub.13, and R.sub.14, independently, is hydrogen, alkyl, haloalkyl, hydroxyalkyl, alkoxy, hydroxy, or amino; and n is 0, 1, or 2. Also disclosed are a method of treating hypocholesterolemia and a method of screening for an LXR agonist by administering a compound described above, a pharmaceutical composition containing at least one of the compounds described above, and an antibody against 5.alpha., 6.alpha.-epoxycholesterol-3-sulfate or 7-ketocholesterol-3-sulfate.

IT **53216-02-7P**, 7-Ketocholesterol-3-sulfate
(prepn. of steroid derivs. as hypocholesteremic agents)

RN 53216-02-7 USPATFULL
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 2 OF 4 USPATFULL (Continued)



L12 ANSWER 3 OF 4 USPATFULL
ACCESSION NUMBER: 96:91831 USPATFULL
TITLE: Vaccine compositions and method for enhancing an immune response
INVENTOR(S): Daynes, Raymond A., Park City, UT, United States
Araneo, Barbara A., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): University of Utah Research Foundation, Salt Lake City, UT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5562910		19961008
APPLICATION INFO.:	US 1993-123843		19930909 (8)

DISCLAIMER DATE: 20130909
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-13972, filed on 4 Feb 1993, now abandoned And a continuation-in-part of Ser. No. US 1991-779499, filed on 18 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-412270, filed on 25 Sep 1989, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Housel, James C.
ASSISTANT EXAMINER: Krsek-Staples, Julie
LEGAL REPRESENTATIVE: Venable, Baetjer, Howard & Civiletti, LLP
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 43 Drawing Figure(s); 18 Drawing Page(s)
LINE COUNT: 1591
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

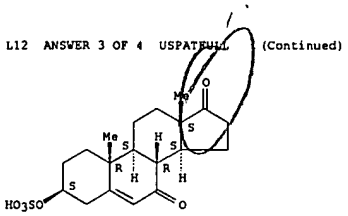
AB The invention relates to a vaccine which comprises an antigen and an immune response augmenting agent. The immune response augmenting agent is capable of enhancing T cell lymphokine production. Suitable immune response augmenting agents include, but are not limited to, dehydroepiandrosterone (DHEA) and DHEA-derivatives. Examples of DHEA derivatives include DHEA-sulfate (DHEA-S), 16.alpha.-bromo-DHEA, 7-oxo-DHEA, 16.alpha.-bromo-DHEA-S and 7-oxo-DHEA-S.

The invention also relates to a method for enhancing a vaccine-induced humoral immune response which comprises administering a vaccine which comprises an antigen and an immunomodulator. The immunomodulator may be an immune response augmenting agent, a lymphoid organ modifying agent or a mixture of the immune response augmenting agent and lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include, but are not limited to, 1,25-dihydroxy Vitamin D.sub.3, biologically active Vitamin D.sub.3 derivatives which are capable of activating the intracellular Vitamin D.sub.3 receptor, all trans-retinoic acid, retinoic acid derivatives, retinol, retinol derivatives and glucocorticoid. Alternatively, the method for enhancing a vaccine-induced humoral immune response comprises separately administering the immunomodulator and a vaccine containing an antigen.

IT **4121-96-4**
(vaccine comprises antigen and immunomodulator or lymphoid organ modifying agent)
RN 4121-96-4 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 3 OF 4 USPATFULL (Continued)



L12 ANSWER 4 OF 4 USPATFULL
ACCESSION NUMBER: 96:43382 USPATFULL
TITLE: Vaccine compositions and method for induction of mucosal immune response via systemic vaccination
INVENTOR(S): Daynes, Raymond A., Park City, UT, United States
Araneo, Barbara A., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): University of Utah Research Foundation, Salt Lake City, UT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5518725		19960521
APPLICATION INFO.:	US 1993-123844		19930909 (8)

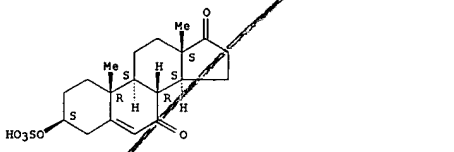
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-13972, filed on 4 Feb 1993, now abandoned And a continuation-in-part of Ser. No. US 1991-779499, filed on 18 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-412270, filed on 25 Sep 1989, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Sidberry, Hazel F.
ASSISTANT EXAMINER: Krsek-Staples, Julie
LEGAL REPRESENTATIVE: Venable, Baetjer, Howard & Civiletti
NUMBER OF CLAIMS: 63
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 56 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 1760
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a vaccine which comprises an antigen and a lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include 1,25-dihydroxy Vitamin D.sub.3, biologically active Vitamin D.sub.3 derivatives which are capable of activating the intracellular Vitamin D.sub.3 receptor, all trans-retinoic acid, retinoic acid derivatives, retinol, retinol derivatives and glucocorticoid. The vaccine composition may further comprise an immune response augmenting agent which enhances T cell lymphokine production. Suitable immune response augmenting agents include dehydroepiandrosterone (DHEA) and DHEA-derivatives. Examples of DHEA derivatives include DHEA-sulfate (DHEA-S), 16-.alpha.-bromo-DHEA, 7-oxo-DHEA, 16-.alpha.-Br-DHEA-S and 7-oxo-DHEA-S. The invention also relates to a method for inducing an antigen-specific mucosal immune response in a vertebrate animal which comprises administering a vaccine which comprises an antigen and a lymphoid organ modifying agent with or without an immune response augmenting agent to a site which drains into a peripheral lymphoid compartment.

IT **4121-96-4**, 7-Oxo-5,6-dehydroepiandrosterone sulfate
(vaccine compns. and method for induction of mucosal immune response via systemic vaccination)
RN 4121-96-4 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 4 OF 4 USPATFULL (Continued)



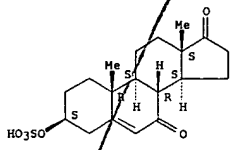
=> d ibib ab hitstr 1-38

L13 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:963688 CAPLUS
DOCUMENT NUMBER: 138:28973
TITLE: Cosmetic preparations containing new derivatives of 7-oxo-DHEA
INVENTOR(S): Dalko, Maria; Cavezza, Alexandre; Picard-Lesboueyries, Elisabeth; Renault, Beatrice; Burnier, Veronique
PATENT ASSIGNEE(S): L'oreal, Fr.
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1266649	A1	20021218	EP 2002-291404	20020606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
FR 2826011	A1	20021220	FR 2001-7804	20010614
JP 2003026697	A2	20030129	JP 2002-173449	20020613

PRIORITY APPLN. INFO.: FR 2001-7804 A 20010614
OTHER SOURCE(S): MARPAT 138:28973
AB Cosmetic prepns. contg. new derivs. of 7-oxo-DHEA (I) for improving the appearance of keratinic materials or prevention or treatment of skin aging, skin pigmentations, hyperseborrhea, and hair loss are claimed. Synthesis of I and cosmetic prepns. contg. I are disclosed.
IT **4121-96-4**
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(cosmetic prepns. contg. new derivs. of 7-oxo-DHEA)
RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

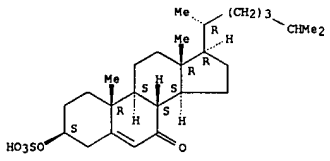
L13 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:658663 CAPLUS
DOCUMENT NUMBER: 137:196688
TITLE: Ecdysone receptor fusion proteins and their use in regulation of gene expression
INVENTOR(S): Palli, Subba Reddy; Kapitskaya, Marianna Zinovjevna; Cress, Dean Ervin
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 102 pp., Cont.-in-part of Appl. No. PCT/US01/09050.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002119521	A1	20020829	US 2001-965703	20010926
WO 2001070816	A2	20010927	WO 2001-US9050	20010321
WO 2001070816	A3	20020829		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-191355P P 20000322
US 2001-269799P P 20010220
WO 2001-US9050 A2 20010321
OTHER SOURCE(S): MARPAT 137:196688
AB A novel inducible gene expression system and methods of modulating gene expression in a host cell is described for applications such as gene therapy, large scale prodn. of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic plants and animals. More specifically, this invention relates to a novel ecdysone receptor/invertebrate retinoid X receptor-based inducible gene expression system and methods of modulating gene expression in a host cell for applications such as gene therapy, large-scale prodn. of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic organisms. This invention relates to a novel inducible gene expression system and methods of modulating gene expression in a host cell for applications such as gene therapy, large scale prodn. of proteins and antibodies, cell-based high throughput screening assays, functional genomics, and regulation of traits in transgenic plants and animals. The transactivation and DNA-binding domains of transcription regulatory factors are sepd. by placing them on two different protein cassettes, resulting in greatly reduced background activity in the absence of a ligand and significantly increased activity over background in the presence of a ligand. The improved gene expression system comprises two chimeric gene expression cassettes; the first encoding a DNA-binding domain fused to a nuclear receptor polypeptide and the second encoding a transactivation domain fused to a nuclear receptor polypeptide.

L13 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)
Interaction of the first protein with the second protein effectively tethers the DNA-binding domain to the transactivation domain. Since the DNA-binding and transactivation domains reside on two different mols., the background activity in the absence of ligand is greatly reduced. Specific embodiments of the invention provide ecdysone receptor ligand-binding domains fused to the DNA-binding domains of GAL4 or LexA, and the ligand-binding domains of retinoid X receptor fused to the VP16 transactivation domain. Truncation mutations in retinoid X receptor or ecdysone receptor modulate the ligand-binding activity.
IT **53216-02-7**, 7-Ketocholesterol-3-sulfate
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulation of gene expression by; ecdysone receptor fusion proteins and their use in regulation of gene expression)
RN 53216-02-7 CAPLUS
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



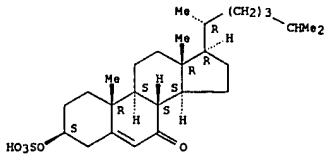
L13 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:658237 CAPLUS
DOCUMENT NUMBER: 137:196635
TITLE: Novel substitution variants of nuclear receptors and their use in a dual switch inducible system for regulation of gene expression
INVENTOR(S): Palli, Subba Reddy; Kapitskaya, Marianna Zinovjevna
PATENT ASSIGNEE(S): Rohm and Haas Company, USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066615	A2	20020829	WO 2002-US5708	20020220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2001-269799P P 20010220
US 2001-313908P P 20010821
OTHER SOURCE(S): MARPAT 137:196635
AB Novel substitution mutant of nuclear receptors, specifically Group H nuclear receptors, that show improved ligand responsiveness that can be used to modulate gene expression in a host cell for applications such as gene therapy, large scale prodn. of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic organisms. In particular, one gene expression cassette is inducibly regulated by a steroid ligand and the other gene expression cassette is inducibly regulated by a non-steroid ligand. Specific embodiments of the invention provide ecdysone receptor ligand-binding domains fused to the DNA-binding domains of GAL4 or LexA, and the ligand-binding domains of retinoid X receptor or ultraspiracle protein fused to the VP16 transactivation domain. A series of substitution mutants of insect ecdysteroid receptors were prepd. by std. PCR mutagenesis and tested for their responsiveness to ecdysteroid induction of reporter gene expression in the dual switch system. Variants that showed increased responsiveness to the ecdysteroids with decreased responsiveness to non-steroid ligands were identified. Variants showed increased responsiveness to both classes of effectors, or to nonsteroids but not ecdysteroids, were also identified.
IT **53216-02-7**, 7-Ketocholesterol-3-sulfate
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulation of receptor function and gene expression by; novel substitution variants of nuclear receptors and their use in dual switch inducible system for regulation of gene expression)
RN 53216-02-7 CAPLUS
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



L13 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:658234 CAPLUS
DOCUMENT NUMBER: 137:196680
TITLE: Substitution variants of nuclear receptors and their use in a dual switch inducible system for regulation of gene expression
INVENTOR(S): Palli, Subba Reddy; Kumar, Mohan Basavaraju; Cress, Dean Ervin; Fujimoto, Ted Tsutomu
PATENT ASSIGNEE(S): Rohm and Haas Company, USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066612	A2	20020829	WO 2002-US5090	20020220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-269799P P 20010220
US 2001-313925P P 20010821
OTHER SOURCE(S): MARPAT 137:196680

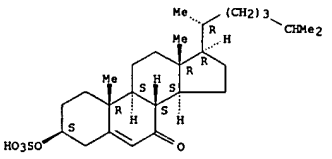
AB This invention relates to the field of biotechnol. or genetic engineering. A mechanism for the regulation of gene expression that allows tight control of a no. of genes is described. The transactivation and DNA-binding domains of transcription regulatory factors are sepd. by placing them on two different protein cassettes. The transactivation and DNA-binding domains of transcription regulatory factors are sepd. by placing them on two different fusion proteins. The chimeric genes encoding the fusion proteins encode a first protein that is a DNA-binding domain fused to a nuclear receptor and the second encoding a transactivation domain fused to a nuclear receptor polypeptide. Interaction of the first protein with the second protein effectively tethers the DNA-binding domain to the transactivation domain. Since the DNA-binding and transactivation domains reside on two different mols., the background activity in the absence of ligand is greatly reduced. Novel substitution mutant of nuclear receptors, specifically Group H nuclear receptors, that show improved ligand responsiveness that can be used to modulate gene expression in a host cell for applications such as gene therapy, large scale prodn. of proteins and antibodies, cell-based high throughput screening assays, functional genomics and regulation of traits in transgenic organisms. In particular, one gene expression cassette is inducibly regulated by a steroid ligand and the other gene expression cassette is inducibly regulated by a non-steroid ligand. Specific embodiments of the invention provide ecdysone receptor ligand-binding domains fused to the DNA-binding domains of GAL4 or LexA, and the ligand-binding domains of retinoid X receptor or ultraspiracle protein

L13 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)

fused to the VP16 transactivation domain. A series of substitution mutants of insect ecdysteroid receptors were prepd. by std. PCR mutagenesis and tested for their responsiveness to ecdysteroid induction of reporter gene expression in the dual switch system. Variants that showed increased responsiveness to the ecdysteroids with decreased responsiveness to non-steroid ligands were identified. Variants showed increased responsiveness to both classes of effectors, or to nonsteroids but not ecdysteroids, were also identified.

IT **53216-02-7**, 7-Ketocholesterol-3-sulfate
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulation of gene expression by; substitution variants of nuclear receptors and their use in dual switch inducible system for regulation of gene expression)
RN 53216-02-7 CAPLUS
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:595508 CAPLUS
DOCUMENT NUMBER: 137:155109
TITLE: Preparation of steroid derivatives for treating hypocholesterolemia
INVENTOR(S): Liao, Shutsung; Song, Ching
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002107233	A1	20020808	US 2002-72128	20020208
WO 2002062302	A2	20020815	WO 2002-US3826	20020207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

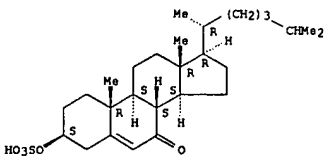
PRIORITY APPLN. INFO.: US 2001-267493P P 20010208
OTHER SOURCE(S): MARPAT 137:155109

AB The steroid derivs. I [R1, R2, R4, R4', R7, R11, R12, R15, R16, R17, R17' = H, OH, amino, carboxyl, oxo, halo, sulfonic acid, -O-sulfonic acid, or alkyl that is optionally inserted with Y; Y = -NH-, -N(alkyl)-, -O-, -S-, -SO-, -SO2-, -O-SO2-, -SO2-O-, -SO3-O-, -CO-, -CO-O-, -O-CO-, -CO-NH-, -CO-N(alkyl)-, -NH-CO-, or -N(alkyl)-CO-, and further optionally substituted with OH, halo, amino, carboxyl, sulfonic acid, or -O-sulfonic acid; R3 = X-Y; X = H, amino, carboxyl, halo, sulfonic acid, -O-sulfonic acid, alkyl; R5R6 = O, double bond; R8, R9, R10, R13, R14 = H, alkyl, haloalkyl, hydroxyalkyl, alkoxy, hydroxy, amino; n = 0-2], or their salts were prepd. Thus, 5.alpha., 6.alpha.-epoxycholesterol-3-sulfate (II) was prepd. by the reaction of 5.alpha.,6.alpha.-epoxy-3.beta.-hydroxycholestane and tri-ethylamine-sulfur trioxide complex (also prepd.). Also disclosed are a method of treating hypocholesterolemia and a method of screening for an LXR agonist by administering I, a pharmaceutical compn. contg. at least one of the compds. described above, and an antibody against II or 7-ketocholesterol-3-sulfate.

IT **53216-02-7P**, 7-Ketocholesterol-3-sulfate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of steroid derivs. as hypocholesteremic agents)
RN 53216-02-7 CAPLUS
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



L13 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2003 ACS

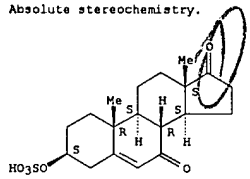
ACCESSION NUMBER: 2002:498448 CAPLUS
DOCUMENT NUMBER: 137:303980
TITLE: Analysis of ergosteroids VIII: Enhancement of signal response of neutral steroidal compounds in liquid chromatographic-electrospray ionization mass spectrometric analysis by mobile phase additives
AUTHOR(S): Marwah, Ashok; Marwah, Padma; Lardy, Henry
CORPORATE SOURCE: Institute for Enzyme Research and Department of Biochemistry, University of Wisconsin, Madison, WI, 53705, USA
SOURCE: Journal of Chromatography, A (2002), 964(1-2), 137-151
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The signal response of moderately polar to nonpolar neutral steroidal compds. in pos. ion mode was significantly improved in electrospray ionization mode by addn. of volatile org. acids (trifluoroacetic acid, acetic and formic) at concns. much lower than those normally employed for HPLC sepns. of ionic compds. Each of the three acids enhanced the sensitivity, the order being: formic acid (.apprx.50-200 ppm, vol./vol.) > acetic acid (100-500 ppm) > trifluoroacetic acid (5-20 ppm). Higher concns. caused decrease in the sensitivity. The extent of increase in the sensitivity was compd. specific and also depended on the nature of org. modifier present in the mobile phase. Acetic acid was the acid of choice for the 'wrong-way-round' ionization of sulfate conjugates. The postcolumn addn. of silver nitrate produced highly stable (M + Ag)+ adducts with concomitant increase in signal response and redn. in baseline noise.

IT **4121-96-4**
RL: ANT (Analyte); ANST (Analytical study)
(enhancement of signal response of neutral steroidal compds. in liq. chromatog.-electrospray ionization mass spectrometric anal. by mobile phase additives)

RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2003 ACS

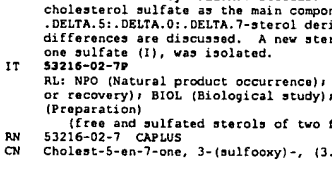
ACCESSION NUMBER: 2002:445845 CAPLUS
DOCUMENT NUMBER: 137:166417
TITLE: Free and sulfated sterols of two far-east Leptasterias starfish
AUTHOR(S): Kapustina, I. I.; Ponomarenko, L. P.; Moiseenko, O. P.; Stonik, V. A.
CORPORATE SOURCE: Pacific Institute of Bioorganic Chemistry, Far-East Division, Russian Academy of Sciences, Vladivostok, 690022, Russia
SOURCE: Chemistry of Natural Compounds (Translation of Khimiya Prirodnykh Soedinenii) (2002), Volume Date 2001, 37(6), 515-519
CODEN: CHNCA8; ISSN: 0009-3130
PUBLISHER: Kluwer Academic/Consultants Bureau
DOCUMENT TYPE: Journal
LANGUAGE: English

AB NMR spectroscopy, capillary GLC, and GLC-MS are used to study the compn. of free and sulfated sterols from the far-east starfish Leptasterias alaskensis asiatica (Fischer) and L. fisheri (Djakonov). The total free sterols of both species are shown to have similar qual. and quant. compns. and contain mainly .DELTA.7-sterols. Sterol sulfate fractions contain cholesterol sulfate as the main component but differ in the ratios of .DELTA.5:.DELTA.0:.DELTA.7-sterol derivs. Possible reasons for these differences are discussed. A new steroid, 3.beta.-hydroxycholest-5-en-7-one sulfate (I), was isolated.

IT **53216-02-7P**
RL: NPO (Natural product occurrence); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(free and sulfated sterols of two far-east Leptasterias starfish)

RN 53216-02-7 CAPLUS
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2003 ACS

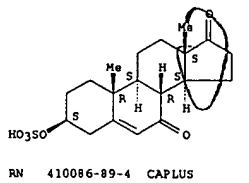
ACCESSION NUMBER: 2002:152200 CAPLUS
DOCUMENT NUMBER: 136:304231
TITLE: Ergosteroids VI. Metabolism of dehydroepiandrosterone by rat liver in vitro: a liquid chromatographic-mass spectrometric study
AUTHOR(S): Marwah, Ashok; Marwah, Padma; Lardy, Henry
CORPORATE SOURCE: University of Wisconsin-Madison, Institute for Enzyme Research and Department of Biochemistry, Madison, WI, 53705-4908, USA
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2002), 767(2), 285-299
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Because relatively large amts. of dehydroepiandrosterone (DHEA) are required to demonstrate its diverse metabolic effects, it is postulated that this steroid may be converted to more active mols. To search for the possible receptor-recognized hormones, DHEA was incubated with whole rat liver homogenate and metabolite appearances were studied by LC-MS as a function of time to predict the sequence of their formation. An array of metabolites has been resolved, identified and characterized by highly specific and accurate technique of LC-MS, and several of these steroids were analyzed quant. Their identities were established by comparison with pure chem. synthesized compds. and by chem. degrdn. of isolated fractions. In the present study, we have reasonably established that DHEA was converted to 7.alpha.-OH-DHEA, 7-oxo-DHEA, and 7.beta.-OH-DHEA in sequence. These metabolites were further reduced at position 7 and/or 17 to form their resp. diols and triols, which were also sulfated at 3.beta.-position. DHEA and its 7-oxygenated derivs. were also converted to their resp. 3.beta.-sulfate esters. Several of these steroids are being reported for the first time. 16.alpha.-Hydroxy-DHEA, androst-5-ene-3.beta.,16.alpha.,17.beta.-triol, androst-4-ene-3,17-dione, 11-hydroxyandrost-4-ene-3,17-dione, androst-5-ene-3,17-diol and testosterone were also identified and characterized. In all, 19 metabolites of DHEA are being reported in this extensive study. We have also detected the formation of 12 addnl. metabolites including several conjugates, which are the subject of current investigation.

IT **4121-96-4 410086-89-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metab. of dehydroepiandrosterone by rat liver in vitro)

RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

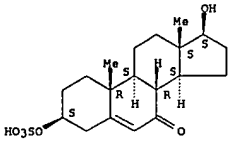
Absolute stereochemistry.



RN 410086-89-4 CAPLUS

L13 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN Androst-5-en-7-one, 17-hydroxy-3-(sulfooxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

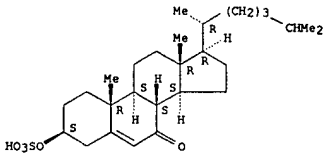


REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:113265 CAPLUS
DOCUMENT NUMBER: 135:75010
TITLE: Auto-oxidized cholesterol sulfates are antagonistic ligands of liver X receptors: implications for the development and treatment of atherosclerosis
AUTHOR(S): Song, C.; Hiipakka, R. A.; Liao, S.
CORPORATE SOURCE: Ben May Institute for Cancer Research, Department of Biochemistry and Molecular Biology, Tang Center for Herbal Medicine Research, University of Chicago, Chicago, IL, 60637, USA
SOURCE: Steroids (2001), 66(6), 473-479
CODEN: STEDAM; ISSN: 0039-128X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Liver X receptors (LXRs) are members of the nuclear receptor superfamily that are involved in regulation of cholesterol transport and metab. Expression of cholesterol 7.alpha.-hydroxylase, cholesteryl ester transfer protein and certain ATP-binding cassette transporters that are responsible for cholesterol efflux from cells is regulated by LXR and its ligands. In this report we show that 5.alpha., 6.alpha.-epoxycholesterol-3-sulfate (ECHS) and 7-ketocholesterol-3-sulfate inhibit transactivation of a reporter gene by LXR. Non-sulfated forms of these compds., as well as many other steroid sulfates, had no antagonistic activity. Using chimeric receptors, the antagonistic activity of ECHS was dependent on its interaction with the ligand-binding domain of LXR. ECHS disrupts recruitment of the co-activator Grip 1 into a complex with agonist-bound LXR and this may be responsible for the obsd. antagonistic properties of these compds. In various cultured cells, these LXR antagonists also promote de novo cholesterol synthesis and apoptosis. 7-Ketocholesterol and 5, 6-epoxycholesterol are present in blood and have been found in atherosclerotic plaques. If sulfated forms of these oxidized sterols are also present, they may have an important role in foam cell formation by inhibiting LXR function. Since LXR agonists can counteract the activity of these antagonists, they may have therapeutic potential against atherosclerosis.
IT **53216-02-7**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(auto-oxidized cholesterol sulfates as antagonistic ligands of liver X receptors in development and treatment of atherosclerosis)
RN 53216-02-7 CAPLUS
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:820640 CAPLUS
DOCUMENT NUMBER: 134:95631
TITLE: Safety and pharmacokinetic study with escalating doses of 3-acetyl-7-oxo-dehydroepiandrosterone in healthy male volunteers
AUTHOR(S): Davidson, Michael; Marwah, Ashok; Sawchuk, Ronald J.; Maki, Kevin; Marwah, Padma; Weeks, Charles; Lardy, Henry
CORPORATE SOURCE: Chicago Center for Clinical Research, Chicago, IL, USA
SOURCE: Clinical and Investigative Medicine (2000), 23(5), 300-310
CODEN: CNVMDL; ISSN: 0147-958X
PUBLISHER: Canadian Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Studies were carried out to evaluate the safety and pharmacokinetics of 3-acetyl-7-oxo-DHEA (3.beta.-acetoxyandrost-5-ene-7,17-dione) given orally. The study consisted of a randomized, double blind, placebo-controlled, escalating dose study in the Chicago Center for Clin. Research involving 22 healthy men. The participants received placebo or 3-acetyl-7-oxo-DHEA at 50 mg/d for 7 days followed by a 7-day washout; 100 mg/d for 7 days followed by a 7-day washout; and 200 mg/d for 28 days. Safety parameters, evaluated at each dose level, included measurement of total testosterone, free testosterone, dihydrotestosterone, estradiol, cortisol, thyroxine and insulin levels. Analyses for 7-oxo-DHEA-3.beta.-sulfate (DHEA-S), the only detectable metabolic product of the administered steroid, were conducted on plasma drawn from all subjects at 0.25, 0.5, 1, 2, 4, 6 and 12 h after the final 100 mg dose of 3.beta.-acetyl-7-oxo-DHEA. There were no differences in the clin. lab. values or in reported minor adverse experiences, between treatment and placebo groups. In general, blood hormone concns. were unaffected by the treatment with 3.beta.-acetyl-7-oxo-DHEA and remained within the normal range. No changes in vital signs, blood chem. or urinalysis occurred during treatment with 3.beta.-acetyl-7-oxo-DHEA compared to placebo. The administered steroid was not detected in the blood but was rapidly converted to 7-oxo-DHEA-S, the concns. of which were proportional to dose. This steroid sulfate did not accumulate; plasma concns. 12 h after the 3.beta.-acetyl-7-oxo-DHEA dose at 7 and 28 days on the 200 mg/d dose were 15.8 and 16.3 .mu.g/L resp. The mean time to peak plasma level of 7-oxo-DHEA-S was 2.2 h; the mean half life was 2.17 h. The apparent clearance averaged 172 L/h, and the apparent mean vol. of distribution was 540 L. These results indicate that 3.beta.-acetyl-7-oxo-DHEA is safe and well tolerated in normal healthy men at doses up to 200 mg/d for 4 wk.
IT **4121-96-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(dehydroepiandrosterone acetyloxo derive safety and pharmacokinetics and metab. and endocrine effects in men)
RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2002 BEILSTEIN CDS MDL

Beilstein Records (BRN):	7361394
Chemical Name (CN):	benzoic acid 17-(1,5-dimethyl-hexyl)-3-methanesulfonyloxy-13-methyl-7-oxo-1,2,3,4,7,8,9,11,12,13,14,15,16,17-tetradecahydro-cyclopenta<a>phenanthren-10-ylmethyl ester
Autonom Name (AUN):	benzoic acid 17-(1,5-dimethyl-hexyl)-3-methanesulfonyloxy-13-methyl-7-oxo-1,2,3,4,7,8,9,11,12,13,14,15,16,17-tetradecahydro-cyclopenta<a>phenanthren-10-ylmethyl ester
Molec. Formula (MF):	C35 H50 O6 S
Molecular Weight (MW):	598.84
Lawson Number (LN):	10581, 9328, 2705
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	2276069
Tautomer ID (TAUTID):	6990701
Beilstein Citation (BSO):	5-09
Entry Date (DED):	1996/05/06
Update Date (DUPD):	1996/05/08

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Atom/Bond Notes:
1. CIP Descriptor: S
2. CIP Descriptor: R

Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	3
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
ED	Entry Date	1
UPD	Update Date	1
ORP	Optical Rotatory Power	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2

L9 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2002 BEILSTEIN CDS MDL (Continued)

RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

Optical Rotatory Power:

Value (ORP) (deg)	Type (.TYP)	Concentr. (.C)	Solvent (.SOL)	Wavelen. (.W) (nm)	Temp. (.T) (Cel)	Ref.
-118	[alpha]	1.46 g/100ml	CHCl3	589	20	1

Reference(s):
1. Fajkos,F., Joska,J., Collect.Czech.Chem.Commun., CODEN: CCCCAK, 43, <1978>, 1142-1151

Reaction:
RX

Reaction ID:	4401638
Reactant BRN:	7360505, 506297
Reactant:	7-Oxo-5-cholesten-3.beta.,19-diol-19-monobenzoat, methanesulfonyl chloride
Product BRN:	7361394
Product:	7-Oxo-5-cholesten-3.beta.,19-diol-3-methansulfonat-19-benzoat
No. of Reaction Details:	1

Reaction Details:
RX

Reaction RID:	4401638.1
Reaction Classification:	Preparation
Reagent:	Py

Reference(s):
1. Fajkos,F., Joska,J., Collect.Czech.Chem.Commun., CODEN: CCCCAK, 43, <1978>, 1142-1151

Reaction:
RX

Reaction ID:	4409908
Reactant BRN:	7361394
Reactant:	7-Oxo-5-cholesten-3.beta.,19-diol-3-methansulfonat-19-benzoat
Product BRN:	7360012
Product:	7-Oxo-3,5-cholestadien-19-ol-19-benzoat
No. of Reaction Details:	1

Reaction Details:
RX

Reaction RID:	4409908.1
Reaction Classification:	Preparation
Reagent:	collidine

Reference(s):
1. Fajkos,F., Joska,J., Collect.Czech.Chem.Commun., CODEN: CCCCAK, 43, <1978>, 1142-1151

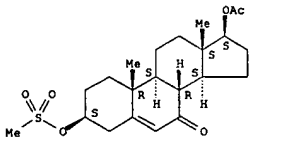
L9 ANSWER 1 OF 1 BEILSTEIN COPYRIGHT 2002 BEILSTEIN CDS MDL (Continued)

Q D1. C 69

2

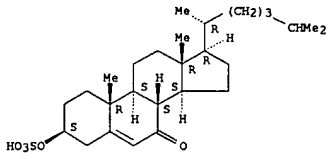
L13 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:510091 CAPLUS
DOCUMENT NUMBER: 89:110091
TITLE: Abnormal elimination reactions of 3.beta.,17.beta.-diacetoxy-5.beta.,6.beta.-epoxyandrostan-7.beta.-ol
AUTHOR(S): Hanson, James R.; Johnson, Alan W.; Kaplan, Maria A. C.
CORPORATE SOURCE: Sch. Mol. Sci., Univ. Sussex, Brighton, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1978), (3), 263-7
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reaction of 3.beta.,17.beta.-diacetoxy-5.beta.,6.beta.-epoxyandrostan-7.beta.-ol (I) with POCl3 gave 3.beta.,17.beta.-diacetoxyandrost-5-en-7-one, whereas the reaction of I with MeSO2Cl/SO2 gave 17.beta.-acetoxy-3.beta.-methylsulfonyloxyandrost-5-en-7-one. Normal products were obtained with 5.alpha.,6.alpha.-epoxy-7.alpha.-ols and in the absence of a 3.beta.-substituent.
IT **66917-34-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 66917-34-8 CAPLUS
CN Androst-5-en-7-one, 17-(acetyloxy)-3-[(methylsulfonyl)oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



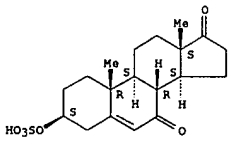
L13 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:461503 CAPLUS
DOCUMENT NUMBER: 81:61503
TITLE: Cholesterol sulfate. I. Occurrence and possible biological function as an amphipathic lipid in the membrane of the human erythrocyte
AUTHOR(S): Bleau, Gilles; Bodley, Frank H.; Longpre, Jacques; Chapdelaine, Alcide; Roberts, Kenneth D.
CORPORATE SOURCE: Dep. Biochem., Univ. Montreal, Montreal, QC, Can.
SOURCE: Biochimica et Biophysica Acta (1974), 352(1), 1-9
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cholesterol sulfate is a normal constituent of human erythrocytes with a concn. approx. 2-fold higher than that of plasma cholesterol sulfate. In these cells, the major fraction of the cholesterol sulfate is firmly bound to the membrane. Cholesterol sulfate as well as certain analogs can protect the erythrocyte against hypotonic hemolysis. This effect is produced in vitro at physiol. concns. of the sterol sulfate, and both the sulfate moiety as well as the side chain of the mol. are necessary for biol. activity.
IT **53216-02-7**
RL: BIOL (Biological study)
(in hemolysis resistance)
RN 53216-02-7 CAPLUS
CN Cholest-5-en-7-one, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



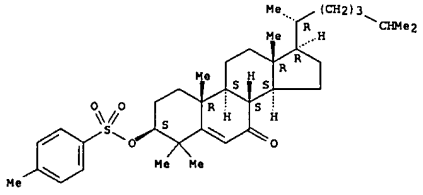
L13 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1972:124618 CAPLUS
DOCUMENT NUMBER: 76:124618
TITLE: Androsta-3,5-diene-7,17-dione. Isolation from urine and formation from 7-keto-dehydroepiandrosterone sulfate under various conditions of hydrolysis
AUTHOR(S): Schubert, K.; Wehrberger, K.; Hobe, G.
CORPORATE SOURCE: Cent. Inst. Microbiol. Exp. Ther., German Acad. Sci. Berlin, Jena, Fed. Rep. Ger.
SOURCE: Endocrinologia Experimentalis (1971), 5(4), 205-10
CODEN: ENEXAM; ISSN: 0013-7200
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Androsta-3,5-diene-7,17-dione (I) (5-7 .mu.g/day) was isolated from the urine of normal men. The properties of 3.beta.-hydroxy-androst-5-ene-17-one-3-sulfate, Na salt (II) under various conditions of hydrolysis (continuous ether extn. of acidified soln., enzymic cleavage with the sulfatase contg. prepn., acetic ester-solvolysis) were: (1) II appeared to be a sulfate conjugate resistant to hydrolysis; (2) a complex hydrolysis may be achieved only at a high concn. of H2SO4. During this process 1 part of this compd. is converted into I. With the aid of a sulfatase-contg. prepn. a true hydrolysis without formation of artificial products takes place.
IT **4121-96-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of, androstadienedione formation in)
RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1970:32117 CAPLUS
DOCUMENT NUMBER: 72:32117
TITLE: Stereochemistry. XXX. Elimination reactions. 4. Solvolysis of keto-tosylates and hydride migration
AUTHOR(S): Abad, Aurelien; Allard, Michel; Levisalles, Jacques
CORPORATE SOURCE: Lab. Chim. Org., Fac. Sci., Nancy, Fr.
SOURCE: Bulletin de la Societe Chimique de France (1969), (4), 1236-44
CODEN: BSCFAS; ISSN: 0037-8968
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The acetolysis of 3.beta.-(tosyloxy)-4,4-dimethylcholest-5-en-7-one, as well as the reaction of PCl5 with 3.beta.-hydroxy-4,4-dimethylcholest-5-en-7-one occurred without ring contraction. The PCl5 treatment of 3.beta.-hydroxy-4,4-dimethyl-5.alpha.-cholestan-7-one (I) gave a small amt. of ring-contraction products. Deuteration expts. showed C-3- to C-4 and C-5 to C-3 hydride shift. A C-3 to C-4 hydride shift was also obsd. during the acetolysis of 3.beta.-(tosyloxy)-4,4-dimethyl-5.alpha.-cholestane and 3.beta.-(tosyloxy)-4,4-dimethyl-5.alpha. -androstane, and the PCl5 treatment of the corresponding 3.beta.-hydroxy derivs. The low yield of ring contraction products during the reaction of I with PCl5 is attributed to delocalization of the pos. charge towards C-5 i n cation (II).
IT **24634-39-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 24634-39-7 CAPLUS
CN Pregn-5-en-7-one, 3.beta.-hydroxy-4,4-dimethyl-, p-toluenesulfonate (8CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1968:444105 CAPLUS
DOCUMENT NUMBER: 69:44105
TITLE: Steroids of unnatural configuration. Synthesis and properties of ring .beta. modified 17.alpha.-20 ketopregnanes
AUTHOR(S): Rubin, Mordecai B.; Brown, Albert P.
CORPORATE SOURCE: Carnegie Inst. of Technol., Pittsburgh, PA, USA
SOURCE: Journal of Organic Chemistry (1968), 33(7), 2794-801
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English

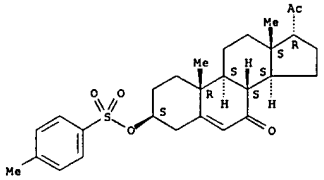
AB 17.alpha.-Pregnenolone acetate (I) served as starting material for synthesis of a series of 17.alpha.-6,20- and 17.alpha.-7,20-dioxopregnanes. The corresponding 17.beta. compds. were also prepd. The effect of C-17 configuration on optical rotation and N.M.R. and mass spectra was investigated. 28 references.

IT **16649-42-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 16649-42-6 CAPLUS

CN 17.alpha.-Pregn-5-ene-7,20-dione, 3.beta.-hydroxy-, p-toluenesulfonate (8CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1967:82716 CAPLUS
DOCUMENT NUMBER: 66:82716
TITLE: Biogenesis of free and sulfated 7.alpha.-hydroxyandrostenolone in subcellular fractions of rat liver
AUTHOR(S): Starka, Lubos; Doellefeld, Erich; Breuer, Heinz
CORPORATE SOURCE: Poliklin., Chirurgischen Universitaetsklin., Bonn, Fed. Rep. Ger.
SOURCE: Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie (1967), 348(3), 293-302
CODEN: HSZPAZ; ISSN: 0018-4888
DOCUMENT TYPE: Journal
LANGUAGE: German

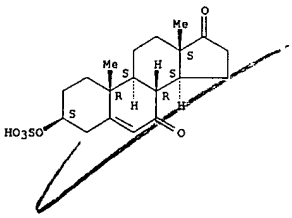
AB Androstenediol, 7.alpha.-hydroxyandrostenolone, and 7.alpha.-hydroxyandrostenediol were produced when androstenolone was incubated with rat liver microsomal fractions. Rat liver microsomal fractions metabolized androstenolone sulfate to androstenediol 3.beta.-monosulfate, 7.alpha.-hydroxyandrostenolone 3.beta.-monosulfate, and 7.alpha.-hydroxyandrostenediol 3.beta.-monosulfate. The optimum pH of 7.alpha.-hydroxylation was 7.4. The rate of formation of the 7.alpha.-hydroxylated compds. was 4-5-fold greater with free androstenolone as the substrate than with androstenolone sulfate. When androstenolone was incubated with the cytoplasmic fraction of rat liver, androstenolone sulfate was formed, whereas 7.alpha.-hydroxyandrostenolone yielded 7-oxoandrostenolone sulfate, 7.alpha.-hydroxyandrostenolone 3.beta.-monosulfate, and 7.alpha.-hydroxyandrostenolone 7.beta.-monosulfate. The optimum pH of sulfation ranged from 5.5 to 5.8. The extent of sulfation was about the same for both androstenolone and 7-hydroxyandrostenolone. In vitro, the formation of 7.alpha.-hydroxyandrostenolone 3.beta.-monosulfate from androstenolone proceeds predominantly via 7.alpha.-hydroxyandrostenolone; the pathway which includes the formation of androstenolone sulfate and subsequent 7.alpha.-hydroxylation seems to be of minor quant. importance. 24 references.

IT **4121-96-4**
RL: BIOL (Biological study)
(as 3.beta.-hydroxyandrost-5-en-17-one sulfate metabolite in liver)

RN 4121-96-4 CAPLUS

CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1966:458271 CAPLUS
DOCUMENT NUMBER: 65:58271
ORIGINAL REFERENCE NO.: 65:10899d-e
TITLE: Steroid conjugates in plasma. XIX. Direct and indirect metabolism of intravenously injected 3H- and 35S-labeled androstenolone sulfate
AUTHOR(S): Oertel, Georg W.; Knapstein, Paul; Treiber, Laszlo
CORPORATE SOURCE: Univ. Saarlandes, Homburg, Germany
SOURCE: Z. Physiol. Chem. (1966), 345(4), 221-35
DOCUMENT TYPE: Journal
LANGUAGE: German

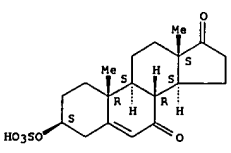
AB cf. CA 65, 4202d. A 22-year-old healthy woman was given an intravenous injection of 0.234 .gamma. Na androstenolone-7-.alpha.-3H sulfate-35S. After 15 min., more than 85% of the radioactivity in the plasma was found in the steroid sulfatide fraction, from which androsterone, 5.beta.-androstanolone, and estrone (with a practically unchanged 3H/35S ratio), as well as other steroids, could be isolated. In the 2-hr. bile were found mainly steroid sulfates with a rapidly increasing 3H/35S ratio. Since the steroid sulfates in the 24-hr. urine exhibited only a slightly increased 3H/35S ratio, the steroid sulfatides formed were probably hydrolyzed to steroid sulfates in the kidney and to free steroids in the liver. Besides a resulfurylation of the free steroid, the conjugation with glucuronic acid in the liver seemed to be of little quantitative importance. 27 references.

IT **4121-96-4**, Androst-5-ene-7,17-dione, 3.beta.-hydroxy-, hydrogen sulfate
(chromatography of)

RN 4121-96-4 CAPLUS

CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1965:490737 CAPLUS
DOCUMENT NUMBER: 63:90737
ORIGINAL REFERENCE NO.: 63:16712c-d
TITLE: An adrenal-secreted "androgen": dehydroisoandrosterone sulfate. Its metabolism and a tentative generalization on metabolism of other steroid conjugates in man
AUTHOR(S): Baulieu, Etienne Emile; Corpechot, Colette; Dray, Fernand; Emiliozzi, Romeo; Lebeau, Marie Claire; Mauvais-Jarvis, Pierre; Robel, Paul
CORPORATE SOURCE: Fac. Med., Paris
SOURCE: Recent Progr. Hormone Res. (1965), 21, 411-94; discussion 494-500
DOCUMENT TYPE: Journal
LANGUAGE: English

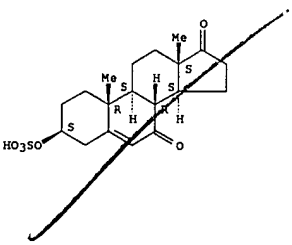
AB A review of the literature and data on dehydroisoandrosterone sulfate (I) secretion by adrenals is presented. Evidence suggests that 7-keto dehydroisoandrosterone sulfate is secreted by adrenal tumors and corticosterone sulfate is secreted in normals. The biol. significance of I comes mainly from its metabolism with probably redefinition of its function as a new type of endocrine secretion. Known urinary metabolites do not account for a 100% excretion of hormones, suggesting formation of other steroids both free and conjugated. The steroid conjugates are known to be metabolites with some also being secreted products. 183 references.

IT **4121-96-4**, Androst-5-ene-7,17-dione, 3.beta.-hydroxy-, hydrogen sulfate
(adrenal tumor secretion of)

RN 4121-96-4 CAPLUS

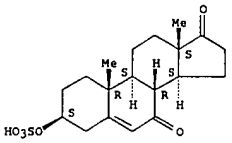
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1962:426038 CAPLUS
DOCUMENT NUMBER: 57:26038
ORIGINAL REFERENCE NO.: 57:5236e-f
TITLE: Conjugated 17-keto steroids in a case of adrenal tumor
AUTHOR(S): Banlieu, Etienne Emile
CORPORATE SOURCE: Fac. Med., Paris
SOURCE: J. Clin. Endo crinol. Metab. (1962), 22, 501-10
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB New chromatographic procedures employed to isolate and identify the free and conjugated 17-keto steroids in an adrenal tumor are described. It was possible to obtain dehydroisoandrosterone as the sulfate ester from the tumor and from peripheral and adrenal venous blood. Free dehydroisoandrosterone could not be detected but both free androstenedione and 11.beta.-hydroxyandrostenedione were found in the tumor. The sulfate esters of androsterone and etiocholanolone could not be isolated from the tumor but were identified in the blood samples. The concns. of etiocholanolone and androsterone sulfates were greater in peripheral venous blood than in adrenal venous blood. Glucuronide esters were not found in the tumor. The isolation of 7-ketodehydroisoandrosterone sulfate from adrenal and peripheral venous plasma was reported.
IT **4121-96-4**, Androst-5-ene-7,17-dione, 3.beta.-hydroxy-, hydrogen sulfate
(chromatography of, from blood plasma in adrenal tumor)
RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

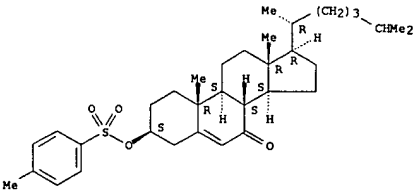
Absolute stereochemistry.



L13 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1962:40001 CAPLUS
DOCUMENT NUMBER: 56:40001
ORIGINAL REFERENCE NO.: 56:7630a-d
TITLE: Steroid derivatives. XII. Chromatography of neutral steroids on a thin aluminum oxide layer
AUTHOR(S): Hermanek, S.; Schwarz, V.; Cekan, Z.
CORPORATE SOURCE: Research Inst. Nat. Drugs, Prague
SOURCE: Collection Czechoslov. Chem. Communs. (1961), 26, 1669-79
DOCUMENT TYPE: Journal
LANGUAGE: German
AB cf. CA 55, 27411c; 56, No. 5.-The use of Al2O3 without binder has the advantage of simplicity in prepg. a thin layer for chromatography. Alk. Al2O3 was used with ligroin (b. 30-50.degree.), benzene, ligroinbenzene, and benzene-EtOH mixts. in various proportions. .DELTA.4-3-Ketones were detected by lightly spraying with SbCl3 in CHCl3, other .DELTA.4-substances with SbCl3 in CHCl3 with 10% SOCl2. Alky. of Al2O3 was without influence on Rf values and, except for formates, trichloroacetates, and trifluoroacetates, did not degrade the substances during the 10-20 min. of development. Benzene was used as the first solvent for unknown mixts. Rf values in several solvents are tabulated for some 90 steroids belonging to 3-substituted cholest-5-enes, 17-substituted 3.beta.-acetoxyandrost-5-enes, 3.beta.substituted androst-5-en-17-ones, 3.beta.-substituted methyl-7keto-eti-5-enates, 3.beta.-substituted cholest-5-en-7-ones, 17.beta.substituted androst-4-en-3-ones, and miscellaneous classes. Chromatographic control of prepn. and purity of a substance is exemplified by the sepn. of pregn-4-ene-17.alpha.,21-diol-3,20-dione, its diacetates, 17.alpha.,21-diacetoxypregn-5-en3.beta.-ol-20-one, and 17.alpha.,21-diacetoxy-3.beta.-formyloxypregn-5en-20-one and accompanying impurities. Adsorptivity of 17.beta.-substituents increased in the following order: COOCH3, OBz, CN-COCH3, OAc, O, OH; for 3.beta.-substituents of cholest-5-ene the order was: H, Cl, OCH3, OAc, OH, and NMe2; similarly, cyclohexylamine moved more slowly than cyclohexanol while aniline was much faster than PhOH.
IT **96772-72-4**, Cholest-5-en-7-one, 3.beta.-hydroxy-, p-toluenesulfonate
(sepn. on Al2O3 film)
RN 96772-72-4 CAPLUS
CN Cholest-5-en-7-one, 3.beta.-hydroxy-, p-toluenesulfonate (7CI) (CA INDEX NAME)

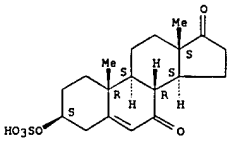
Absolute stereochemistry.

L13 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



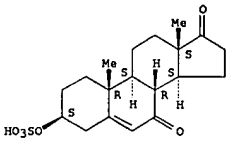
L13 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:145353 CAPLUS
DOCUMENT NUMBER: 55:145353
ORIGINAL REFERENCE NO.: 55:27598c-d
TITLE: Virilizing adrenal tumor. Study of 17-keto steroids in tumor tissue, in adrenal and peripheral blood, and in urine
AUTHOR(S): Guillon, J.; Colas, J.; Trichereau, R.; Delumeau, G.; Baulieu, E. E.
SOURCE: Ann. endocrinol. (Paris) (1961), 22, 331-5
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB 5-conjugated 7-ketodehydroepiandrosterone was isolated from peripheral venous blood and from tumor tissue of a female with virilism.
IT **4121-96-4**, Androst-5-ene-7,17-dione, 3.beta.-hydroxy-, hydrogen sulfate
(in blood and neoplasm in virilism)
RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:94761 CAPLUS
DOCUMENT NUMBER: 55:94761
ORIGINAL REFERENCE NO.: 55:17871f-g
TITLE: Isolation of 5-androstene-7,17-dione-3.beta.-ol sulfuric ester from peripheral blood plasma and adrenal venous plasma
AUTHOR(S): Baulieu, E. E.; Emiliozzi, R.; Corpechot, C.
CORPORATE SOURCE: Fac. med., Paris
SOURCE: Experientia (1961), 17, 110-11
DOCUMENT TYPE: Journal
LANGUAGE: French
AB 5-Androstene-7,17-dione-3.beta.-ol sulfuric ester was isolated from the peripheral venous blood plasma of several virilized women, in adrenal venous plasma of one of them, and also in 3 cases of adrenal tumor.
IT **4121-96-4**, Androst-5-ene-7,17-dione, 3.beta.-hydroxy-, hydrogen sulfate
(in blood plasma in adrenal disorder)
RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



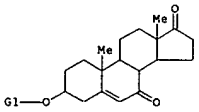
=> d ibib ab fqhit 1-30

L15 ANSWER 1 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 138:28973 MARPAT
TITLE: Cosmetic preparations containing new derivatives of 7-oxo-DHEA
INVENTOR(S): Dalko, Maria; Cavezza, Alexandre; Picard-Lesboueyries, Elisabeth; Renault, Beatrice; Burnier, Veronique
PATENT ASSIGNEE(S): L'oreal, Fr.
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1266649	A1	20021218	EP 2002-291404	20020606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
FR 2826011	A1	20021220	FR 2001-7804	20010614
JP 2003026697	A2	20030129	JP 2002-173449	20020613
PRIORITY APPLN. INFO.:			FR 2001-7804	20010614

AB Cosmetic prepns. contg. new derivs. of 7-oxo-DHEA (I) for improving the appearance of keratinic materials or prevention or treatment of skin aging, skin pigmentations, hyperseborrhea, and hair loss are claimed. Synthesis of I and cosmetic prepns. contg. I are disclosed.

MSTR 1



G1 = SO3H
MPL: claim 1
NTE: substitution is restricted

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)
G3 = 33

G4 = 40

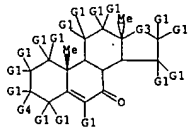
MPL: claim 1
NTE: additional ring formation and substitution also claimed
NTE: or protected derivatives

L15 ANSWER 2 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:385008 MARPAT
TITLE: Process improvements in oxidation of steroids
INVENTOR(S): Burgoyne, David L.; Shen, Yaping; Ji, Guejun; Zhou, Yuanlin; Ramachandran, Kishore; Paschalides, Nicholas D.; Kelleher, Eugene W.
PATENT ASSIGNEE(S): Inflazyme Pharmaceuticals Ltd., Can.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094849	A2	20021128	WO 2002-CA728	20020522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2001-293013P	20010522
OTHER SOURCE(S):		CASREACT 137:385008		

AB Steroids contg. a cyclohexene moiety are efficiently oxidized to the corresponding .alpha.,.beta.-unsatd. ketone using copper iodide and t-Bu hydroperoxide. The steroid contg. the .alpha., .beta.-unsatd. ketone is efficiently converted to the corresponding vicinal diol using a hydroborating reagent followed by oxidative workup, e.g., borane followed by sodium perborate. Benzoyl and substituted benzoyls are superior protecting groups for hydroxyl groups present in the compds. Thus, the androstane deriv. I (R = p-O2NC6H4) was placed in a reactor contg. Me3COOH, CuI and pyridine in CH2Cl2 and MeCN the mixt. agitated at room temp. for 1-2 h and then heated to 45.degree. to give 62.5% II after workup, II was treated with borane/THF at -5-0.degree. untill TLC indicated the absence of starting material and then NaBO3 added to give 69 % III after workup.

MSTR 1

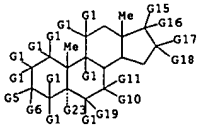


L15 ANSWER 3 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:329452 MARPAT
TITLE: Compositions with a non-glucocorticoid steroid and/or a ubiquinone and kit for treatment of respiratory and lung disease
INVENTOR(S): Nyce, Jonathan.W.
PATENT ASSIGNEE(S): Epigenesis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085297	A2	20021031	WO 2002-US12555	20020422
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2001-286124P	20010424

AB A pharmaceutical or veterinary compn. comprises as the active agent (i) a non-glucocorticoid steroid or its analog, and (ii) a ubiquinone or their salts, in an amt. effective for reducing levels of, or hypersensitivity to, adenosine, increasing levels of lung surfactant or ubiquinone, or for preventing or treating respiratory, lung and cancer diseases. The present treatment is useful for treating asthma, rhinitis, COPD, CF, RDS, pulmonary fibrosis, cancer and other diseases. For example, a metered dose inhaler contained ubiquinone 200 mg, dehydroepiandrosterone (DHEA) 200 mg, a stabilizer 5.0 .mu.g, trichlorofluoromethane 23.70 mg, and dichlorodifluoromethane 61.25 mg.

MSTR 2A



G5 = SH
G10+G11= O
MPL: claim 1
NTE: or pharmaceutically or veterinarily acceptable salts
NTE: substitution is restricted
NTE: additional ring and oxo formation also claimed

L15 ANSWER 3 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)

L15 ANSWER 4 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:242464 MARPAT
TITLE: Treatment of tumors with steroids that interrupt disturbances in Wnt signaling or provide an angiostatic effect
INVENTOR(S): Hagstroem, Tomas
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072003	A2	20020919	WO 2002-SE443	20020311

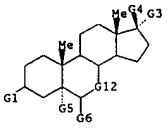
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 2001-857 20010313

AB The present invention relates to steroid derivs. for use as medicaments. More specifically, the invention also relates to the use of a steroid deriv. of 5-androstene-, 5-pregnenolone or corresponding satd. derivs. (androstane- or pregnane-) in the manuf. of a medicament for the treatment of a benign and/or malignant tumor, which medicament is capable of interrupting disturbances in Wnt-signaling, such as cell-cycle arrest in G1-phase, and/or providing an angiostatic effect. Examples of such steroid derivs. are .DELTA.-5-androstene-17.alpha.-ol, androstane-17.alpha.-ol, or pregnane-17.alpha.-ol derivs. In a further aspect, the invention relates to a method of producing a medicament for the treatment of a benign and/or malignant tumor and/or an inflammatory condition comprising the steps of contacting 5-androstane-3.beta..alpha.,17.alpha.-diol or androstane-3.beta..alpha.-diol, an enzyme and a sulfotransferase to provide 5-androstene-17.alpha.-ol-3.beta.-sulfate or corresponding androstane deriv. (17.alpha.-AEDS or 17-AADS); and mixing the 17.alpha.-AEDS or 17.alpha.-AADS so produced with a suitable carrier; whereby a medicament which is capable of acting as a ligand to peroxisome proliferator-activated receptor-.gamma. (PPAR.gamma.) is produced. Pharmaceutical compns. contg. the steroids plus other nuclear receptor ligands are also claimed.

MSTR 1

L15 ANSWER 4 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G1 = 26

G7 = SO3H
G12 = 41

G13 = O
MPL: claim 1
NTE: substitution is restricted

L15 ANSWER 5 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 137:155109 MARPAT
TITLE: Preparation of steroid derivatives for treating hypocholesterolemia
INVENTOR(S): Liao, Shutsung; Song, Ching
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

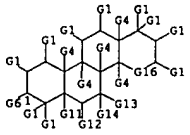
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002107233	A1	20020808	US 2002-72128	20020208
WO 2002062302	A2	20020815	WO 2002-US3826	20020207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-267493P 20010208

AB The steroid derivs. I [R1, R2, R4, R4', R7, R11, R12, R15, R16, R17, R17' = H, OH, amino, carboxyl, oxo, halo, sulfonic acid, -O-sulfonic acid, or alkyl that is optionally inserted with Y; Y = -NH-, -N(alkyl)-, -O-, -S-, -SO-, -SO2-, -O-SO2-, -SO2-O-, -SO3-O-, -CO-, -CO-O-, -O-CO-, -CO-NH-, -CO-N(alkyl)-, -NH-CO-, or -N(alkyl)-CO-, and further optionally substituted with OH, halo, amino, carboxyl, sulfonic acid, or -O-sulfonic acid; R3 = X-Y; X = H, amino, carboxyl, halo, sulfonic acid, -O-sulfonic acid, alkyl; R5R6 = O, double bond; R8, R9, R10, R13, R14 = H, alkyl, haloalkyl, hydroxyalkyl, alkoxy, hydroxy, amino; n = 0-2], or their salts were prepd. Thus, 5.alpha., 6.alpha.-epoxycholesterol-3-sulfate (II) was prepd. by the reaction of 5.alpha.,6.alpha.-epoxy-3.beta.-hydroxycholestane and tri-ethylamine-sulfur trioxide complex (also prepd.). Also disclosed are a method of treating hypocholesterolemia and a method of screening for an LXR agonist by administering I, a pharmaceutical compn. contg. at least one of the compds. described above, and an antibody against II or 7-ketocholesterol-3-sulfate.

MSTR 1



G7 = S
G13+G14= O

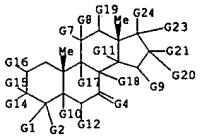
L15 ANSWER 5 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)
MPL: claim 1
NTE: substitution is restricted

L15 ANSWER 6 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 136:129430 MARPAT
TITLE: Preparation of meiosis regulating compounds for use as contraceptives or compounds to treat infertility
INVENTOR(S): Gronvald, Frederick Christian; Faarup, Peter; Guddal, Erling
PATENT ASSIGNEE(S): Den.
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 436,810, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002013302	A1	20020131	US 2001-878884	20010611
WO 9700884	A1	19970109	WO 1996-DK273	19960621
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
ZA 9605333	A	19970123	ZA 1996-5333	19960624
PRIORITY APPLN. INFO.:			DK 1995-728	19950623
			DK 1995-730	19950623
			DK 1995-1461	19951222
			WO 1996-DK273	19960621
			US 1997-973661	19971219
			US 1999-436810	19991109

AB Sterol deriv. compds., structurally related to natural compds. which can be extd. from bull testes and from human follicular fluid, useful for regulating meiosis in oocytes and in male germ cells. Some of these compds. are useful in the treatment of infertility, whereas other compds. are useful as contraceptives.

MSTR 1E



G4 = O
G14 = OSO3H
MPL: claim 1
NTE: additional methylene, oxo, hydroximino, ring, and double bond

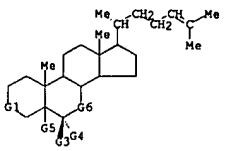
L15 ANSWER 6 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)
formation also claimed
NTE: substitution is restricted

L15 ANSWER 7 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 134:193624 MARPAT
TITLE: Highly stereoselective synthesis of 24R,25- and 24S,25- dihydroxysteroid
INVENTOR(S): Zhou, Xiangdong; Zhou, Weishan
PATENT ASSIGNEE(S): Shanghai Inst. of Organic Chemistry, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 12 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1254716	A	20000531	CN 1999-124007	19991112
CN 1098273	B	20030108		
PRIORITY APPLN. INFO.:			CN 1999-124007	19991112

OTHER SOURCE(S): CASREACT 134:193624
AB An improved Sharpless asym. dihydroxylation method was used for the synthesis of 24R,25- and 24S,25- dihydroxysteroids from .DELTA.24-steroids I. .DELTA.24-Steroids I was defined as [R1 or R2 = MOMO, THPO, OAc, OCH2CH2O, OH, H, PhCOO, MeSO2O, TsO, O, TBDMS, Bn; R3 = .alpha.- or .beta.-H, or R3 R4 is double bond, R4 or R5 = MOMO, THP, OAc, OCH2CH2O, OH, H, PhCOO, MeSO2O, or TsO, O; R4R5 = O, R6 or R7 = MOM, THP, OAc, OCH2CH2O, OH, H, PhCOO, MeSO2O, TsO, O, R6R7 = O;]. The title compds II. [R1, R2, R3, R4, R5, R6, R7, same as defined in I, R8 = .alpha.- or .beta.-OH;] were preped from I, reacting with K3Fe(CN)6, K2CO3, CH3SO2NH2 in mixed solvent t-butanol-water, under the temp. 0.degree. to room temp. in the presence of catalyst K2OsO2(OH)4 and (DHQD)2PHAL or (DHQ)2PHAL, then adding the second solvent (such as THF, DMF, DME, acetonitrile, t-butylmethyl ether, acetone, etc.), reacting over 10-20 h. Thus, K3Fe(CN)6, K2CO3, MeSO2NH2, (DHQD)2PHAL, and K2OsO2(OH)4 were mixed with 3-5 mL t-butanol and 3-5 mL H2O, cooled down the temp. to 0.degree., after stirring 20 min, (5.beta.)-3.alpha.,6.alpha.-Di(methoxymethoxy)choles-24-ene in diisopropyl ether was added, continuing stirring over 16 h under the temp. 0.degree. to room temp. until the starting material disappeared. Keeping the temp. at 0.degree., adding NaSO3, stirring 30 min at room temp., then adding Et acetate, 2N KOH, 15% HCl, washed with satd. NaHCO3 and NaCl, dried with anhyd. NaSO4, evapg. solvent, giving the foaming solid crude product, after column chromatog., giving (5.beta.)-3.alpha.,6.alpha.-Di(methoxymethoxy)cholesta-24R,25-diol with 85% yield, d.e. 99.74%.

MSTR 1A



G1 = 40

L15 ANSWER 7 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)

G2 = OSO2Me
G6 = C(O)
MPL: claim 1

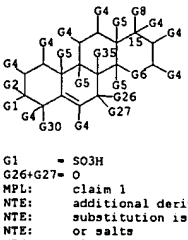
L15 ANSWER 8 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:350394 MARPAT
TITLE: Preparation of steroid derivatives
INVENTOR(S): Liao, Shutsung; Song, Ching
PATENT ASSIGNEE(S): Arch Development Corporation, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066611	A1	20001109	WO 2000-US11243	20000427
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1189922	A1	20020327	EP 2000-928431	20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010197	A	20020716	BR 2000-10197	20000427
JP 2002543216	T2	20021217	JP 2000-615640	20000427
NO 2001005314	A	20011227	NO 2001-5314	20011030
PRIORITY APPLN. INFO.:			US 1999-131728P	19990430
			US 2000-191864P	20000324
			WO 2000-US11243	20000427

AB The steroid derivs. I (R3 = H, amino, carboxyl, oxo, halo, sulfonic acid, -O-sulfonic acid, or alkyl that is optionally inserted with -NH-,-N(alkyl)-, -O-, -S-, -SO-, -SO2-, -O-SO2-, -SO2-O-, -O-SO3-, -SO3-O-, -CO-, -CO-O-, -O-CO-, -CO-NH-, -CO-N(alkyl)-, -NH-CO-, or -N(alkyl)-CO-, and further optionally substituted with hydroxy, halo, amino, carboxyl, sulfonic acid, or -O-sulfonic acid),. R1, R2, R4, R4', R6, R7, R11, R12, R15, R16, and R17', independently, is H, hydroxy, amino, carboxyl, oxo, halo, sulfoic acid, -O-sulfonic acid, or alkyl that is optionally inserted with -NH-, -N(alkyl)-, -O-, -S-, -SO-, -SO2-, -O-SO2-, -SO2-O-, -O-SO3-, -SO3-O-, -CO-, -CO-O-, -O-CO-, -CO-NH-, -CO-N(alkyl)-, -NH-CO-, or -N(alkyl)-CO-, and further optionally substituted with hydroxy, halo, amino, carboxyl, sulfonic acid, or -O-sulfonic acid. R5, R8, R9, R10, R13, and R14, independently, is H, alkyl, haloalkyl, hydroxyalkyl, alkoxy, hydroxy, or amino; R17 is -X-Y-Z, in which X is a bond, or alkyl or alkenyl, optionally inserted with -NH-, -N(alkyl)-, -O-, or -S-, and further optionally forming a cyclic moiety with R16 and the 2 ring carbon atoms to which R16 and R17 are bonded; Y is -CO-, -SO-, -SO2-, -O-SO2-, -SO2-O-, -O-SO3-, -SO3-O-, -CO-O-, -O-CO-, -CO-NH-,-CO-N(alkyl)-, -NH-CO-, -N(alkyl)-CO-, or a bond. Z = alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, or heteroaralkyl, and is optionally substituted with hydroxy, alkoxy, amino, halo, sulfonic acid, -O-sulfonic acid, carboxyl, oxo, alkyloxycarbonyl, alkylcarbonyloxy, alkylaminocarbonyl, alkylcarbonylamino, alkylcarbonyl, alkylsulfinyl, alkylsulfonyl, or

L15 ANSWER 8 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)
alkylthio; or is -CH(A)-B with A being a side chain of an amino acid, and B being hydrogen, -NRaRb, or -COORc wherein each of Ra, Rb, and Rc, independently, is hydrogen or alkyl; n is 0, 1, or 2. Provided that when Z is substituted with carboxyl or alkyloxycarbonyl, Y is a bond and either X or Z contains at least one double bond, and that when Y is a bond, either X is -NH-alkyl, -NH-alkenyl, -N(alkyl)-alkyl-, -N(alkyl)-alkenyl-, -O-alkyl-, -O-alkenyl-, -S-alkyl-, or -S-alkenyl-; or Z is substituted with halo, sulfonic acid, -O-sulfonic acid, alkylsulfinyl, or alkylsulfonyl, or is alkenyl or their salts were prepd. Thus, to a stirred soln. of L- (or D-) phenylalanine ester hydrochloride in dry DMF was added triethylamine and the mixt. was stirred at room temp. for 10 min, bile acid and 1-ethyl-3-[3-dimethylaminopropyl]-carbodiimide were then added and the suspension was stirred at room temp. overnight. Reaction mixt. was dild. with water and Et acetate, the org. layer was sepd. and the water layer was extd. with Et acetate again, the combined org. layer was then washed with 1N HCl, water, 1N NaOH and water, and dried (MgSO4), removed the solvent under reduced pressure to afford the steroid derivs., e.g. II. Steroid derivs. of I interact with nuclear liver X receptor (LXR) and ubiquitous receptor (UR), and can be used to treat a variety of LXR- or UR- mediated disorders.

MSTR 1C



G1 = SO3H
G26+G27= O
MPL: claim 1
NTE: additional derivatization also claimed
NTE: substitution is restricted
NTE: or salts
NTE: also incorporates claims 18, 35 and 49

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

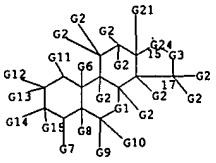
L15 ANSWER 9 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:68934 MARPAT
TITLE: Cytokine combination therapy for indications of immunodeficiency
INVENTOR(S): Prendergast, Patrick T.
PATENT ASSIGNEE(S): Hollis-Eden Pharmaceuticals, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035472	A2	20000622	WO 1999-IB2001	19991215
WO 2000035472	A3	20001109		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1998-112206P	19981215

AB This invention relates to methods of treatment of persons and animals with indications of immunodeficiency, wherein the the indication is resultant from viral and/or retroviral, bacterial, fungal or parasitic infection and/or plus infectious protein units. The method involves the administration of an agonist or antagonist to Th2 cytokines in combination with antiviral agents or immune-enhancing agents. In one aspect of the invention, the agonist or antagonist is a receptor to interleukin-4 (or mutein receptor) which is administered in combination with an antiviral agent. Preferred antiviral/immune-enhancing agents include (a) compds. having a steroid skeleton (e.g. dehydroepiandosterone), and metabolites, analogs and precursors thereof, and pharmaceutically acceptable salts of any such compds., metabolites, analogs and precursors; (b) protease inhibitors; and (c) reverse transcriptase inhibitors. Also described is a method of enhancing viral replication as a means of exposing latent infection by the administration of an agonist or antagonist to a Th2 cytokine. Further provided are such methods comprising administering to a patient at least one Th2 cytokine and at least one agonist and/or at least one antagonist to said Th2 cytokine. There are also provided compns. and kits for use in such methods, as well as the use of such compds. in the manuf. of medicaments for treatment for various conditions.

MSTR 1

L15 ANSWER 9 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G1 = C(O)
G3 = 26

G15 = SCN
G24 = 184

DER: or metabolites, analogs, precursors or salts
MPL: claim 1

L15 ANSWER 10 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:34421 MARPAT
TITLE: Use of 17-ketosteroid compounds and derivatives, metabolites, and precursors thereof in treatment of toxoplasmosis and cryptosporidiosis
INVENTOR(S): Ahlem, Clarence Nathaniel; Frincke, James Martin; Prendergast, Patrick T.; Thadikonda, Krupakar Paul
PATENT ASSIGNEE(S): Hollis-Eden Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

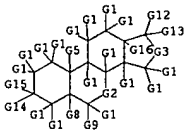
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032176	A2	20000608	WO 1999-US28080	19991124
WO 2000032176	A3	20001207		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-110127P 19981127
US 1999-124087P 19990311
US 1999-126056P 19990323

AB 17-Keto steroids and related compds., e.g. 16.alpha.-bromoepiandrosterone (I), and their pharmaceutically acceptable salts are used to treat infections with Toxoplasma or Cryptosporidium and to ameliorate or reduce symptoms assocd. with such infections. Thus, a suspension was prepd. contg. 50 mg I/mL in PEG-300 25, EtOH 12.5, benzyl benzoate 5, and propylene glycol 5%. I.v. administration of the steroids is preferred. The keto steroids may also be used to treat, or to ameliorate symptoms assocd. with, retroviral infections or malaria in humans.

MSTR 1A



G2 = C(O)
G3 = 45

L15 ANSWER 10 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)

G27 = S
MPL: claim 1
NTE: further derivatization also claimed

L15 ANSWER 11 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:22443 MARPAT
TITLE: 17-Ketosteroids and derivatives, metabolites and precursors in the treatment of hepatitis C virus and other togaviruses
INVENTOR(S): Ahlem, Clarence Nathaniel; Frincke, James Martin; Prendergast, Patrick T.
PATENT ASSIGNEE(S): Hollis-Eden Pharmaceuticals, Inc., USA; Colthurst Ltd
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032177	A2	20000608	WO 1999-US28082	19991124
WO 2000032177	A3	20010322		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 9915644	A	20010807	BR 1999-15644	19991124
EP 1133287	A2	20010919	EP 1999-965050	19991124

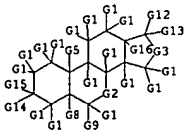
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1998-109924P 19981124
US 1999-124087P 19990311
US 1999-126056P 19990323
WO 1999-US28082 19991124

AB The invention provides the use of 17-ketosteroids, as well as derivs., metabolites and precursors of such compds., and their pharmaceutically acceptable salts, in the treatment of prevention of hepatitis C type virus and/or hepatitis G type virus in patients in need of such treatment. In addn., the invention provides methods to treat or prevent togavirus infections, including infections by 1 or more alphaviruses, flaviviruses, such as yellow fever virus, hepatitis C virus and hepatitis G virus, rubella viruses, or pestiviruses, such as bovine virus diarrhea virus. In addn., the invention provides combination therapies including administration of one or more compd. of the present invention, as defined herein, and administration of one or more compd. selected from plasma concn.-enhancing compds., macrophage stimulating factor, oxidn. agents, ribavirin and alpha-interferon, and/or oxygen ventilation. The compds. of the present invention may also be used to ameliorate or reduce 1 or more symptoms assocd. with a togavirus infection. Two lots of a non-aq. formulation was made at a 16a-bromoepiandrosterone concn. of 50 mg/mL in 25% polyethylene glycol 300, 12.5% dehydrated EtOH, 5% benzyl benzoate, and 57.5% propylene glycol.

MSTR 1A

L15 ANSWER 11 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)

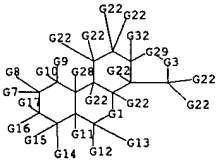


G2 = C(O)
G3 = 45

G27 = S
MPL: claim 1
NTE: further derivatization also claimed

L15 ANSWER 12 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)
assocd. with any infection or condition disclosed herein. Formulations for compds. of the invention are also claimed and exemplified.

MSTR 1



G1 = C(O)
G3 = 22

G17 = 240

G29 = 210

DER: and salts, metabolites, analogs, precursors, hydrates, tautomers, ionized forms and solvates
MPL: claim 1
NTE: additional double bond, and oxo and methylidene formation also claimed
STE: and stereoisomers and positional isomers

L15 ANSWER 12 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 133:13157 MARPAT
TITLE: Use of 17-ketosteroid compounds and derivatives, metabolites and precursors thereof in the treatment of malaria and the treatment of African and American trypanosomiasis
INVENTOR(S): Ahlem, Clarence Nathaniel; Frincke, James Martin; Prendergast, Patrick T.
PATENT ASSIGNEE(S): Hollis-Eden Pharmaceuticals, Inc., USA; Colthurst Ltd
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032201	A2	20000608	WO 1999-US28079	19991124
WO 2000032201	A3	20001221		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356539	AA	20000608	CA 1999-2356539	19991124
BR 9915623	A	20010814	BR 1999-15623	19991124
EP 1135138	A2	20010926	EP 1999-960591	19991124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002531407	T2	20020924	JP 2000-584896	19991124
PRIORITY APPLN. INFO.:			US 1998-109923P	19981124
			US 1999-124087P	19990311
			US 1999-126056P	19990323
			WO 1999-US28079	19991124

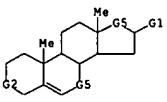
AB The invention provides the use of 17-ketosteroid compds., as well as derivs., metabolites and precursors of such compds., and pharmaceutically acceptable salts of any of these compds., collectively defined herein as the "compds. of the present invention", in the treatment of malaria, African Trypanosomiasis and American Trypanosomiasis, or to ameliorate or reduce one or more symptoms assocd. with a Plasmodium or Trypanosoma infection. The present invention is further directed to the use of such compds. in the treatment or prevention of one or more kind of parasites and/or one or more diseases caused by such parasites, against one or more kind of Mycoplasma and/or one or more diseases caused by such Mycoplasmas and/or against one or more of the following indications or infections: (a) hairy Leukoplakia, (b) oral candidosis, (c) mouth ulcerations-aphthous/herpetic/bacterial, (d) fungal candida, (e) human papilloma virus, (f) molluscum contagiosum, (g) squamous oral carcinoma, (h) Kaposi's sarcoma oral lesions, (i) periodontitis, (j) necrotizing gingivitis, (k) orafacial herpes zoster, and (l) rotaviruses, as well as all other indications and infections. The compds. of the present invention may also be used to ameliorate or reduce one or more symptoms

L15 ANSWER 13 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:282021 MARPAT
TITLE: Method for reducing central nervous system impairment
INVENTOR(S): Araneo, Barbara A.; McKay, Lawrence
PATENT ASSIGNEE(S): Pharmadigm, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952532	A1	19991021	WO 1999-US7319	19990402
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9934676	A1	19991101	AU 1999-34676	19990402
PRIORITY APPLN. INFO.:			US 1998-59184	19980414
			WO 1999-US7319	19990402

AB The present invention is related to a method for reducing central nervous system (CNS) impairment, such as results from an ischemic event caused by a stroke or trauma to the central nervous system. In accordance with the present invention, CNS impairment is reduced by administering a dehydroepiandrosterone (DHEA) congener as soon as possible after the ischemic event.

MSTR 1



G2 = 96

G3 = SH
G5 = 94 / C(O)

DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: additional spiro ring and enol formation also disclosed

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 131:98052 MARPAT
TITLE: Method using a dehydroepiandrosterone derivative for enhancing or accelerating re-epithelialization or re-endothelialization of a tissue
INVENTOR(S): Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

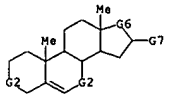
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5929060	A	19990727	US 1996-695769	19960801
US 5532230	A	19960702	US 1994-284688	19940809
US 5686438	A	19971111	US 1995-480748	19950607
JP 10147526	A2	19980602	JP 1996-301826	19961113
US 5922701	A	19990713	US 1997-901085	19970728
WO 9805338	A2	19980212	WO 1997-US12954	19970731
WO 9805338	A3	19980326		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738917	A1	19980225	AU 1997-39817	19970731
AU 713850	B2	19991209		
EP 915702	A2	19990519	EP 1997-936184	19970731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002514168	T2	20020514	JP 1998-507972	19970731
AT 216242	E	20020515	AT 1997-936184	19970731
ES 2174275	T3	20021101	ES 1997-936184	19970731

PRIORITY APPLN. INFO.:
US 1992-877612 19920501
US 1993-29422 19930309
US 1993-152002 19931110
US 1994-284688 19940809
US 1995-480748 19950607
US 1995-483524 19950607
WO 1994-US2558 19940308
US 1996-695769 19960801
US 1997-869177 19970605
US 1997-901085 19970728
WO 1997-US12954 19970731

AB A method is provided for enhancing or accelerating re-epithelialization or re-endothelialization of a tissue. Examples of re-epithelialization in which the invention is particularly suited include, but are not limited to, re-epithelialization of (a) skin following surgical wounds, (b) skin abrasions caused by mech. trauma, caustic agents or burns, (c) cornea following cataract surgery or corneal transplants, (d) mucosal epithelium (respiratory, gastrointestinal, genitourinary, mammary, oral cavity, ocular tissue, liver and kidney) following infection, nonpathol. etiologies or drug therapy, (e) skin following grafting and (f) renal

L15 ANSWER 14 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)
tubule following acute tubular necrosis. Examples of re-endothelialization in which the invention is particularly suited include, but are not limited to, re-endothelialization (or regrowth of endothelium) in blood vessels following angioplasty, and the lysis of fibrin clots or lysis or mech. disruption of thrombi in coronary arteries. In accordance with the invention, the time to complete re-epithelialization or re-endothelialization is enhanced or accelerated by administering a dehydroepiandrosterone (DHEA) deriv.

MSTR 1



G2 = 32 / C(O)

G3 = SH
G6 = 64

DER: or pharmaceutically acceptable monosaccharides, disaccharides or oligosaccharides derivatives
MPL: claim 2

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 15 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:76173 MARPAT
TITLE: Method using dehydroepiandrosterone derivative for reducing mast cell-mediated allergic reactions
INVENTOR(S): Dowell, Tad; Norton, Steven D.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA; Pharmadigm, Inc.
SOURCE: U.S., 20 pp., Cont.-in-part of U.S. Ser. No. 870,234.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

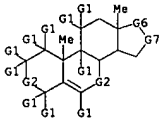
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5859000	A	19990112	US 1997-966385	19971107
US 5811418	A	19980922	US 1995-480747	19950607
US 5846963	A	19981208	US 1995-516540	19950818
US 5753640	A	19980519	US 1995-580716	19951229
US 5977095	A	19991102	US 1997-870234	19970605
CA 2308406	AA	19990520	CA 1998-2308406	19981030
WO 9924039	A1	19990520	WO 1998-US23038	19981030
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9912895	A1	19990531	AU 1999-12895	19981030
AU 736614	B2	20010802		
EP 1033989	A1	20000913	EP 1998-956356	19981030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001522803	T2	20011120	JP 2000-520131	19981030

PRIORITY APPLN. INFO.:
US 1995-480747 19950607
US 1995-516540 19950818
US 1995-580716 19951229
US 1997-870234 19970605
US 1993-29422 19930309
US 1994-284688 19940809
US 1995-480744 19950607
US 1995-480745 19950607
US 1995-480748 19950607
US 1997-966385 19971107
WO 1998-US23038 19981030

AB A method is provided for reducing mast cell-mediated allergic reactions, including mast cell-mediated allergy and asthma. Mast cell-mediated allergic reactions, including type I hypersensitivity response to allergens and asthma, are reduced by administering a dehydroepiandrosterone deriv. to a patient in a manner which quickly raises blood levels of the active agent.

MSTR 1

L15 ANSWER 15 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G2 = 32 / C(O)

G3 = SH
G6 = 64

G7 = 97

DER: or pharmaceutically acceptable monosaccharides, disaccharides or oligosaccharides derivatives
MPL: claim 1
NTE: substitution is restricted
NTE: additional ring formation also claimed

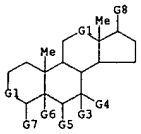
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:43296 MARPAT
TITLE: Immunomodulating, bile-derivable compositions for the treatment of viral disorders
INVENTOR(S): Percheson, Paul
PATENT ASSIGNEE(S): Imutec Pharma Inc., Can.
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9852585	A1	19981126	WO 1998-CA494	19980522
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2238460	AA	19981123	CA 1998-2238460	19980522
AU 9875160	A1	19981211	AU 1998-75160	19980522
ZA 9806224	A	19990429	ZA 1998-6224	19980713
PRIORITY APPLN. INFO.:			CA 1997-2206047	19970523
			WO 1998-CA494	19980522

AB The present invention relates to the use of a compn. exhibiting antiviral properties, comprising small mol. wt. components of less than 3000 daltons, and having the following properties: (a) is extractable from bile of animals; (b) is capable of stimulating monocytes and macrophages in vitro and in vivo; (c) is capable of modulating tumor necrosis factor prodn.; (d) contains no measurable IL-1.alpha., IL-1.beta., TNF, IL-6, IL-8, IL-4, GM-CSF or IFN-.gamma.; (e) shows no cytotoxicity to human peripheral blood mononuclear cells or lymphocytes; and (f) is not an endotoxin. The invention also relates to the use of the antiviral compn. when used in conjunction with other drugs such as antiviral compds. or immunomodulators such as interferon.

MSTR 1



G1 = 23

L15 ANSWER 16 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)

HC—G2
23

G2 = OSO3H
G3 +G4 = O
MPL: claim 23

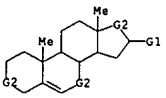
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 130:17243 MARPAT
TITLE: Vaccine compositions and method for enhancing an immune response
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 38 pp., Cont.-in-part o f U. S. 5,562,910.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5837269	A	19981117	US 1995-487173	19950607
US 5562910	A	19961008	US 1993-123843	19930909
US 5827841	A	19981027	US 1994-295068	19940920
US 5753237	A	19980519	US 1994-309704	19940921
US 5919465	A	19990706	US 1994-309717	19940921
PRIORITY APPLN. INFO.:			US 1989-412270	19890925
			US 1991-779499	19911018
			US 1993-13972	19930204
			US 1993-123843	19930909
			US 1993-18471	19930216
			US 1994-219418	19940329

AB The invention relates to a vaccine which comprises an antigen and an immune response-augmenting agent. The immune response-augmenting agent is capable of enhancing T cell lymphokine prodn. Suitable immune response augmenting agents include, but are not limited to, DHEA, DHEA-derivs. and DHEA congeners. The invention also relates to a method for enhancing a vaccine-induced humoral immune response which comprises administering a vaccine which comprises an antigen and an immunomodulator. The immunomodulator may be an immune response augmenting agent, a lymphoid organ modifying agent or a mixt. of the immune response augmenting agent and lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include, but are not limited to, 1,25-dihydroxy Vitamin D3, 25-hydroxy Vitamin D3, biol. active 1,25-dihydroxy Vitamin D3, derivs. which are capable of activating the intra-cellular Vitamin D3 receptor, all trans-retinoic acid, retinoic acid derivs., retinol, retinol derivs. and glucocorticoid. Alternatively, the method for enhancing a vaccine-induced humoral immune response comprises sep. administering the immunomodulator and a vaccine contg. an antigen.

MSTR 1



G2 = C(O) / 21

HC—G3
21

L15 ANSWER 17 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)

G3 = SH
DER: and pharmaceutically acceptable salts
MPL: claim 1

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

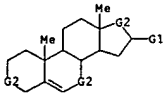
L15 ANSWER 18 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:239907 MARPAT
TITLE: Methods for preventing progressive tissue necrosis, reperfusion injury, bacterial translocation and adult respiratory distress syndrome using DHEA
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. 5,532,230.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811418	A	19980922	US 1995-480747	19950607
US 5532230	A	19960702	US 1994-284688	19940809
US 5846963	A	19981208	US 1995-516540	19950818
US 5753640	A	19980519	US 1995-580716	19951229
US 5977095	A	19991102	US 1997-870234	19970605
US 5859000	A	19990112	US 1997-966385	19971107
US 6150348	A	20001121	US 1999-311282	19990514
US 6187767	B1	20010213	US 1999-311306	19990514
PRIORITY APPLN. INFO.:			US 1993-29422	19930309
			US 1994-284688	19940809
			WO 1994-US2558	19940308
			US 1995-480744	19950607
			US 1995-480745	19950607
			US 1995-480747	19950607
			US 1995-480748	19950607
			US 1995-516540	19950818
			US 1995-580716	19951229
			US 1997-870234	19970605

AB The present invention is directed to a method for preventing or reducing ischemia following injury, such as reperfusion injury following ischemia, cellular damage assocd. with ischemic episodes, such as infarctions or traumatic injuries, and thus to prevent or reduce the consequent progressive necrosis of tissue assocd. with such ischemia. This effect is achieved by administering DHEA, DHEA derivs. or DHEA congeners to a patient as soon as possible after the injury. The present invention is further directed to methods for preventing or reducing bacterial translocation or adult respiratory distress syndrome in a patient. Similarly, bacterial translocation and adult respiratory distress syndrome are prevented or reduced by administering DHEA, DHEA derivs. or DHEA congeners to a patient. DHEA, at concns. of 10.mu.M or greater, prevented the up-regulation of P-selectin expression normally obsd. on endothelium in response to histamine.

MSTR 1

L15 ANSWER 18 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G2 = C(O) / 21

G3 = SH
DER: and pharmaceutically acceptable salts
MPL: claim 1

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:67927 MARPAT
TITLE: Stereoselective synthesis of 24-hydroxylated compounds useful for the preparation of aminosterols, vitamin D analogs, and other compounds
INVENTOR(S): Kinney, William A.; Jones, Steven; Zhang, Xuehai; Rao, Meena N.; Bulliard, Michel; Meckler, Harold; Lee, Nancy
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

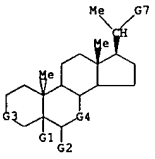
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824800	A2	19980611	WO 1997-US22031	19971208
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6262283	B1	20010717	US 1997-985876	19971205
AU 9855914	A1	19980629	AU 1998-55914	19971208
AU 746559	B2	20020502		
EP 942918	A2	19990922	EP 1997-952256	19971208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001505207	T2	20010417	JP 1998-524012	19971208
US 2002068834	A1	20020606	US 2001-833055	20010412
PRIORITY APPLN. INFO.:			US 1996-32378P	19961206
			US 1997-985876	19971205
			US 1997-985576	19971205
			WO 1997-US22031	19971208

OTHER SOURCE(S): CASREACT 129:67927

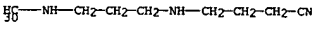
AB A method is described for stereoselectively reducing an unsatd. alkyl ketone substituent attached to a fused ring base. In this method, the unsatd. alkyl ketone reacts with a chiral oxazaborolidine reagent, e.g. I. This reaction stereoselectively reduces the unsatd. alkyl ketone to an unsatd. alkyl alc. The unsatd. alkyl alc. can be further reduced, if desired, to produce a satd. alkyl alc. The fused ring base can be, for example, a steroid ring base or a base of a vitamin D analog. The process in accordance with the invention can be used with an alkenone substituent (e.g., a 22-one-24-one substituent) or an alkynone substituent (e.g., a 22-yne-24-one substituent) on a steroid ring base to make squalamine or other useful aminosterol compds. and intermediates for making aminosterol compds. Thus, II is reduced using I to give the 24S-hydroxy deriv.

MSTR 1

L15 ANSWER 19 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G3 = 30



G4 = C(O)
MPL: claim 19

L15 ANSWER 20 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 129:32295 MARPAT
TITLE: Methods for preventing progressive tissue necrosis, reperfusion injury, bacterial translocation and adult respiratory distress syndrome
INVENTOR(S): Araneo, Barbara A.; Orlinska, Urszula; Farrukh, Imad S.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA; Pharmadigm, Inc.
SOURCE: U.S., 24 pp., Cont.-in-part of U.S. Ser. No. 516,540. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

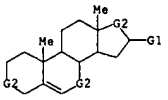
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5753640	A	19980519	US 1995-580716	19951229
US 5587369	A	19961224	US 1995-480744	19950607
US 5635496	A	19970603	US 1995-480745	19950607
US 5686438	A	19971111	US 1995-480748	19950607
US 5811418	A	19980922	US 1995-480747	19950607
US 5846963	A	19981208	US 1995-516540	19950818
US 5977095	A	19991102	US 1997-870234	19970605
US 5859000	A	19990112	US 1997-966385	19971107
US 6150348	A	20001121	US 1999-311282	19990514
US 6187767	B1	20010213	US 1999-311306	19990514

PRIORITY APPLN. INFO.:
US 1995-480744 19950607
US 1995-480745 19950607
US 1995-480747 19950607
US 1995-480748 19950607
US 1995-516540 19950818
US 1993-29422 19930309
US 1994-284688 19940809
US 1995-446568 19950519
US 1995-446569 19950519
US 1995-580716 19951229
US 1997-870234 19970605

AB The present invention is related to a method for preventing or reducing the effects of ischemia. The ischemia may be assocd. with injury or reperfusion injury, such as occurs as a result of infarctions, thermal injury (burns), surgical trauma, accidental trauma, hemorrhagic shock and the like. The invention is also related to methods for preventing or reducing bacterial translocation, adult respiratory distress syndrome, adherence of blood cells and platelets to endothelial cells and pulmonary hypertension. In accordance with the present invention, these conditions are prevented or reduced by administering dehydroepiandrosterone-3-sulfate (DHEAS), DHEA or a DHEA congener.

MSTR 1

L15 ANSWER 20 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G2 = C(O) / 21

G3 = SH
DER: and pharmaceutically acceptable salts
MPL: claim 8

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 21 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:230566 MARPAT
TITLE: Intermediates for the synthesis of vitamin D and steroid derivatives and processes for preparation thereof
INVENTOR(S): Horne, David A.; Kubodera, Noboru; Suzuki, Hiroshi; Shimizu, Hitoshi
PATENT ASSIGNEE(S): Trustees of Columbia University In the City of New York, USA; Chugai Seiyaku Kabushiki Kaisha; Horne, David A.; Kubodera, Noboru; Suzuki, Hiroshi; Shimizu, Hitoshi
SOURCE: PCT Int. Appl., 94 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809935	A1	19980312	WO 1997-US15393	19970903
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9742449	A1	19980326	AU 1997-42449	19970903
EP 931047	A1	19990728	EP 1997-940745	19970903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000514463	T2	20001031	JP 1998-512795	19970903
JP 3310301	B2	20020805		
JP 2002234897	A2	20020823	JP 2001-393683	19970903
US 6399767	B1	20020604	US 2000-576543	20000522

PRIORITY APPLN. INFO.:
US 1996-25361P 19960903
JP 1998-512795 19970903
WO 1997-US15393 19970903
US 1999-254271 19990303

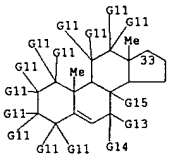
OTHER SOURCE(S): CASREACT 128:230566

AB Compds. of formula I [R1, R2 = alkyl; n = 1-5; W, X = H, alkyl; Y = O, S, (substituted) NH; Z = steroid-17-yl; 9,10-secosteroid-17-yl; CD steroid ring] are prepd. in a process comprizing the reaction of II with an epoxide or alkane in the presence of a base. Thus, NaH was added to 1.alpha.,3.beta.-bis(tert-butyldimethylsilyloxy)-20(S)-hydroxypregna-5,7-diene, then 4-bromo-2,3-epoxy-2-methylbutane was added to give III in 90% yield.

MSTR 1

G6 = 33

L15 ANSWER 21 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G11 = NH2
G13+G14= O
MPL: claim 1
NTE: alkylidene and oxo formation also claimed
NTE: also incorporates claim 18

L15 ANSWER 22 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:176479 MARPAT
TITLE: Use of a dehydroepiandrosterone derivative for enhancing or accelerating re-epithelialization or re-endothelialization of a tissue
INVENTOR(S): Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

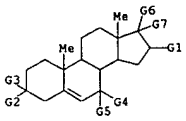
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805338	A2	19980212	WO 1997-US12954	19970731
WO 9805338	A3	19980326		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5929060	A	19990727	US 1996-695769	19960801
US 5922701	A	19990713	US 1997-901085	19970728
AU 9738917	A1	19980225	AU 1997-39817	19970731
AU 713850	B2	19991209		
EP 915702	A2	19990519	EP 1997-936184	19970731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002514168	T2	20020514	JP 1998-507972	19970731
AT 216242	E	20020515	AT 1997-936184	19970731

PRIORITY APPLN. INFO.: US 1996-695769 19960801
US 1997-869177 19970605
US 1997-901085 19970728
US 1992-877612 19920501
US 1993-29422 19930309
US 1993-152002 19931110
US 1994-284688 19940809
US 1995-480748 19950607
US 1995-483524 19950607
WO 1997-US12954 19970731

AB The present invention relates to the use of a dehydroepiandrosterone (DHEA) deriv. as described herein or a pharmaceutically acceptable salt thereof for prepg. a pharmaceutical compn. for accelerating re-epithelialization or re-endothelialization of tissue in a subject in need thereof. Examples of re-epithelialization in which the invention is particularly suited include, but are not limited to, re-epithelialization of (a) skin following surgical wounds; (b) skin abrasions caused by mech. trauma, caustic agents or burns; (c) cornea following cataract surgery or corneal transplants; (d) mucosal epithelium (respiratory, gastrointestinal, genitourinary, mammary, oral cavity, ocular tissue, liver and kidney) following infection, nonpathol. etiologies or drug therapy; (e) skin following grafting; and (f) renal tubule following acute tubular necrosis. Examples of re-endothelialization in which the invention is particularly suited include, but are not limited to,

L15 ANSWER 22 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)
re-endothelialization (or regrowth of endothelium) in blood vessels following angioplasty, and the lysis of fibrin clots or lysis or mech. disruption of thrombi in coronary arteries. In accordance with the present invention, the time to complete re-epithelialization or re-endothelialization is enhanced or accelerated by administering a dehydroepiandrosterone (DHEA) deriv.

MSTR 1



G2 = SH
G4 +G5 = O
DER: and pharmaceutically acceptable salts
MPL: claim 2
NTE: substitution is restricted

L15 ANSWER 23 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 128:154276 MARPAT
TITLE: Preparation of 6,7-oxygenated steroids and therapeutic uses related thereto
INVENTOR(S): Burgoyne, David L.; Shen, Yaping; Langlands, John M.; Rogers, Christine; Chau, Joseph H-L.; Piers, Edward; Salari, Hassan
PATENT ASSIGNEE(S): Inflazyme Pharmaceuticals Ltd., Can.
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

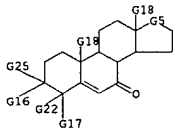
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9802450	A2	19980122	WO 1997-CA490	19970711
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6046185	A	20000404	US 1997-893575	19970710
CA 2259981	AA	19980122	CA 1997-2259981	19970711
AU 9733323	A1	19980209	AU 1997-33323	19970711
AU 722815	B2	20000810		
EP 917534	A2	19990526	EP 1997-929071	19970711
EP 917534	B1	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1222159	A	19990707	CN 1997-195531	19970711
BR 9710353	A	20000111	BR 1997-10353	19970711
JP 2001503732	T2	20010321	JP 1997-535644	19970711
AT 229031	E	20021215	AT 1997-929071	19970711
MX 9900444	A	20000131	MX 1999-444	19990108
KR 2000023661	A	20000425	KR 1999-700116	19990109

PRIORITY APPLN. INFO.: US 1996-23450P 19960711
US 1996-679642 19960712
WO 1997-CA490 19970711

AB Steroid compds. of formula I [R = H, protecting group; positions C1-C17 independently substituted] having various oxygen substitution on the steroid nucleus are disclosed. Steroids having 3,4-epoxy functionality are also disclosed. In addn., steroids having C17 pyran and .delta.-lactone functionality, with oxygen substitution at C6 and C7, or at C15, of the steroid nucleus, are disclosed. Thus, II is prepd. from 4-androsten-3,17-dione in many steps. II showed antithrombolytic, antiallergic and antiasthmatic activity.

MSTR 3

L15 ANSWER 23 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G5 = 27

G19 = 5
DER: and pharmaceutically acceptable salts and solvates
MPL: claim 79
NTE: additional bond and ring formation, and substitution also claimed
NTE: substitution is restricted

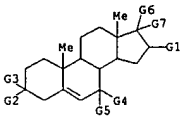
L15 ANSWER 24 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 127:61230 MARPAT
TITLE: Methods for preventing progressive tissue necrosis, reperfusion injury, bacterial translocation and adult respiratory distress syndrome
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. 5,583,126.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5635496	A	19970603	US 1995-480745	19950607
US 5532230	A	19960702	US 1994-284688	19940809
US 5583126	A	19961210	US 1995-446568	19950519
US 5846963	A	19981208	US 1995-516540	19950818
CA 2223739	AA	19961219	CA 1995-2223739	19950908
WO 9640152	A1	19961219	WO 1995-US10990	19950908
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9535413	A1	19961230	AU 1995-35413	19950908
AU 699749	B2	19981210		
EP 835113	A1	19980415	EP 1995-932345	19950908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11124393	A2	19990511	JP 1995-267607	19950908
US 5753640	A	19980519	US 1995-580716	19951229
US 5977095	A	19991102	US 1997-870234	19970605
FI 9704346	A	19980116	FI 1997-4346	19971126
NO 9705717	A	19980204	NO 1997-5717	19971205
US 6150348	A	20001121	US 1999-311282	19990514
US 6187767	B1	20010213	US 1999-311306	19990514

PRIORITY APPLN. INFO.:
US 1993-29422 19930309
US 1994-284688 19940809
US 1995-446568 19950519
WO 1994-US2558 19940308
US 1995-480744 19950607
US 1995-480745 19950607
US 1995-480747 19950607
US 1995-480748 19950607
US 1995-516540 19950818
WO 1995-US10990 19950908
US 1995-580716 19951229
US 1997-870234 19970605

AB The present invention is directed to a method for preventing or reducing ischemia following injury, such as reperfusion injury following ischemia, cellular damage assocd. with ischemic episodes, such as infarctions or traumatic injuries, and thus to prevent or reduce the consequent progressive necrosis of tissue assocd. with such ischemia. This effect is achieved by administering DHEA, DHEA derivs. or DHEA congeners to a patient as soon as possible after the injury. The present invention is further directed to methods for preventing or reducing bacterial translocation or adult respiratory distress syndrome in a patient. Similarly, bacterial translocation and adult respiratory distress syndrome are prevented or reduced by administering DHEA, DHEA derivs. or DHEA congeners to a patient.

MSTR 1



G2 = SH
G4 +G5 = O
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted

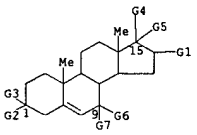
L15 ANSWER 25 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:140219 MARPAT
TITLE: Dehydroepiandrosterone derivatives for preventing progressive tissue necrosis reperfusion injury, bacterial translocation and adult respiratory distress syndrome
INVENTOR(S): Araneo, Barbara A.; Orlinska, Urszula; Farrukh, Imad S.; Daynes, Raymond A.
PATENT ASSIGNEE(S): Paradigm Biosciences, Inc., USA; University of Utah Research Foundation
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640152	A1	19961219	WO 1995-US10990	19950908
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5587369	A	19961224	US 1995-480744	19950607
US 5635496	A	19970603	US 1995-480745	19950607
US 5686438	A	19971111	US 1995-480748	19950607
US 5846963	A	19981208	US 1995-516540	19950818
AU 9535413	A1	19961230	AU 1995-35413	19950908
AU 699749	B2	19981210		
EP 835113	A1	19980415	EP 1995-932345	19950908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
FI 9704346	A	19980116	FI 1997-4346	19971126
NO 9705717	A	19980204	NO 1997-5717	19971205

PRIORITY APPLN. INFO.:
US 1995-480744 19950607
US 1995-480745 19950607
US 1995-480748 19950607
US 1995-516540 19950818
US 1993-29422 19930309
US 1994-284688 19940809
US 1995-446568 19950519
US 1995-446569 19950519
US 1995-480747 19950607
WO 1995-US10990 19950908

AB The present invention is related to a method for preventing or reducing the effects of ischemia. The ischemia may be assocd. with injury or reperfusion injury, such as occurs as a result of infarctions, thermal injury (burns), surgical trauma, accidental trauma, hemorrhagic shock and the like. The invention is also related to methods for preventing or reducing bacterial translocation, adult respiratory distress syndrome, adherence of blood cells and platelets to endothelial cells and pulmonary hypertension. In accordance with the present invention, these conditions are prevented or reduced by administering dehydroepiandrosterone-3-sulfate (DHEAS) or a DHEA congener.

MSTR 1



G2 = SH
G6 +G7 = O
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted

L15 ANSWER 26 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 126:140218 MARPAT
TITLE: Methods for preventing progressive tissue necrosis, reperfusion injury, bacterial translocation and adult respiratory distress syndrome using DHEA, its derivs. and congeners
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. 5,489,581.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

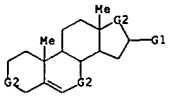
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5587369	A	19961224	US 1995-480744	19950607
US 5532230	A	19960702	US 1994-284688	19940809
US 5489581	A	19960206	US 1995-446569	19950519
US 5846963	A	19981208	US 1995-516540	19950818
CA 2223739	AA	19961219	CA 1995-2223739	19950908
WO 9640152	A1	19961219	WO 1995-US10990	19950908
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9535413	A1	19961230	AU 1995-35413	19950908
AU 699749	B2	19981210		
EP 835113	A1	19980415	EP 1995-932345	19950908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11124393	A2	19990511	JP 1995-267607	19950908
US 5753640	A	19980519	US 1995-580716	19951229
US 5977095	A	19991102	US 1997-870234	19970605
FI 9704346	A	19980116	FI 1997-4346	19971126
NO 9705717	A	19980204	NO 1997-5717	19971205
US 6150348	A	20001121	US 1999-311282	19990514
US 6187767	B1	20010213	US 1999-311306	19990514

PRIORITY APPLN. INFO.:
US 1993-29422 19930309
US 1994-284688 19940809
US 1995-446569 19950519
WO 1994-US2558 19940308
US 1995-480744 19950607
US 1995-480745 19950607
US 1995-480747 19950607
US 1995-480748 19950607
US 1995-516540 19950818
WO 1995-US10990 19950908
US 1995-580716 19951229
US 1997-870234 19970605

AB The present invention is directed to a method for preventing or reducing ischemia following injury, such as reperfusion injury following ischemia, cellular damage assocd. with ischemic episodes, such as infarctions or traumatic injuries, and thus to prevent or reduce the consequent progressive necrosis of tissue assocd. with such ischemia. This effect is

L15 ANSWER 26 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)
achieved by administering DHEA, DHEA derivs. or DHEA congeners to a patient as soon as possible after the injury. The present invention is further directed to methods for preventing or reducing bacterial translocation or adult respiratory distress syndrome in a patient. Similarly, bacterial translocation and adult respiratory distress syndrome are prevented or reduced by administering DHEA, DHEA derivs. or DHEA congeners to a patient.

MSTR 1



G2 = C(O) / 21

G3 = SH
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted

L15 ANSWER 27 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 122:274034 MARPAT
TITLE: Immunomodulating compositions from bile
INVENTOR(S): Rang, Romeo
PATENT ASSIGNEE(S): Imutec Corp., Can.
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

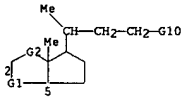
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9507089	A1	19950316	WO 1994-CA494	19940909
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2171281	AA	19950316	CA 1994-2171281	19940909
AU 9476489	A1	19950327	AU 1994-76489	19940909
EP 717631	A1	19960626	EP 1994-926737	19940909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1136777	A	19961127	CN 1994-194002	19940909
JP 09502706	T2	19970318	JP 1994-508370	19940909
NO 9600907	A	19960430	NO 1996-907	19960306
FI 9601109	A	19960506	FI 1996-1109	19960308
AU 9897242	A1	19990304	AU 1998-97242	19981221
AU 732816	B2	20010503		

PRIORITY APPLN. INFO.:
US 1993-118269 19930909
US 1993-155303 19931122
US 1994-231726 19940424
AU 1994-76489 19940909
WO 1994-CA494 19940909

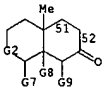
AB A compn. for use as an immunomodulator comprises small-mol.-wt. components (<3000 Da) extractable from bile of animals which (a) are capable of stimulating monocytes and macrophages in vitro; (b) are capable of modulating tumor necrosis factor prodn.; (c) contain no measurable IL-1a, IL-1b, TNF, IL-6, IL-8, IL-4, GM-CSF or IFN-.gamma.; (d) have an anti-proliferative effect in a malignant mouse hybridoma cell line; (e) show no cytotoxicity to human peripheral blood mononuclear cells; and (f) contain no endotoxin. The bile components may include steroids [I; X = H, OH, :O, OSO3H; Y = CHMe(CH2)3R1, CHMe(CH2)2R2; R1 = CHMe2, CHMeCH2OH, CHMeCHO, CO2H; R2 = CH(OH)CHMeCO2H, CO2H, CONHR; R = amino acid residue] and their .DELTA.4, .DELTA.5(6), and .DELTA.6 dehydro derivs., phospholipids, sphingolipids, diglycerides, oligosaccharides, mucin or proteoglycan hydrolysis products, fat-sol. vitamins, glutamic acid conjugates, alkylamines, fatty acids, etc. Thus, bovine gall bladder bile was mixed with an equal vol. of EtOH, centrifuged, optionally treated with activated C, concd. by evapn., and extd. with Et2O, and the aq. phase was buffered, autoclaved, and analyzed by HPLC.

MSTR 1

L15 ANSWER 27 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)



G1 = 51-2 52-5



G2 = CH2 / 96

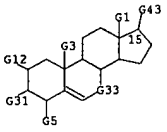
MPL: claim 27

L15 ANSWER 28 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 120:107475 MARPAT
TITLE: preparation of 4-alkenylsterols and analogs as anticholesteremics
INVENTOR(S): Archer, Robert Allen; Beavers, Lisa Selsam; Gadski, Robert Alan; Lin, Ho Shen; McClure, Don B.; McCowan, Jefferson Ray; Pawlak, Joseph Matthew; Rampersaud, Ashraff Ali; Schmidt, Robert John; et al.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 121 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 562849	A2	19930929	EP 1993-302261	19930324
EP 562849	A3	19940216		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9301117	A	19930928	NO 1993-1117	19930325
CA 2092766	AA	19930904	CA 1993-2092766	19930326
AU 9335514	A1	19930930	AU 1993-35514	19930326
HU 64082	A2	19931129	HU 1993-901	19930326
CN 1081682	A	19940209	CN 1993-105203	19930326
JP 06056670	A2	19940301	JP 1993-67968	19930326
ZA 9302178	A	19940926	ZA 1993-2178	19930326
BR 9301342	A	19931005	BR 1993-1342	19930329
PRIORITY APPLN. INFO.:			US 1992-858908	19920327
			US 1993-18985	19930303

AB Title compds. [I; R = OH, acyloxy, NH2, AcNH, etc.; R1 = (halo)alkyl; R2 = H, (halo)methyl; R3 = H, (halo)alkyl, CH2CR6:CR7R8; R4 = H, CH2Ph, (CH2)nX4; R5 = AZZ1X3; A, Z = bond, O, CHMe, CMe(OH), etc.; R6 = H, halo, (halo)alk(en)yl; R7, R8 = H, halo, (halo)methyl; R6R7 = atoms to complete a ring; X = O, H2, H and OH, H and halo, etc.; X3 = H, Ph, OPh, halo, haloalkyl, OH, etc.; X4 = H, OH, (halo) alkyl, (halo)alkoxy, etc.; Z1 = (substituted) alk(en)ylene; n = 1-16; dashed lines = optional position of optional addnl. bond] were prepd. as upregulators of LDL receptor gene expression. Thus, (+)-4-cholesten-3-one was condensed with BrCH2CH:CH2 and the product reduced to give title compd. II which reduced plasma cholesterol levels from 252 to 205 mg/dL in hypercholesteremic African green monkeys receiving 50 mg/kg/day in diet.

MSTR 1D

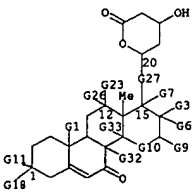


L15 ANSWER 29 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 119:226236 MARPAT
TITLE: Preparation of hydroxytetrahydro-2H-pyranonyl steroids having hypocholesterolemic properties
INVENTOR(S): McGarry, Daniel G.; Volz, Francis A.; Regan, John R.; Chang, Michael N.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: U.S., 26 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5216015	A	19930601	US 1991-650494	19910205
PRIORITY APPLN. INFO.:			US 1991-650494	19910205

AB Title compds. I (R1 = Me or part of double bond; R2 = H, alkyl, aryl, aralkyl; R3 = H, alkyl, part of double bond; R2R3 = spiro group; R4, R5 = H, alkyl, aralkyl, aryl; W = carbalkoxy, carboaryloxy, H, HO, alkoxy, aralkyloxy, etc.; W' = H, part of double bond; WW' = O, some provisos; X = carbalkoxy, carboaryloxy, carboaralkoxy, H, HO, alkoxy, aryloxy, etc.; X' = H, XX' = O; Y = carbalkoxy, aryloxy, H, HO, (alkyl-), (dialkyl-) amino, H2NCH2, etc.; Y' = H; YY' = O; Z = RaCH, RaCHCHRa, RaCHRbCHRcC, etc., wherein Ra, Rb, Rc = H, alkyl; n = 0, 1), are prepd. Cholic acid treated with MeI gave Me cholate which in 5 steps was converted to 17.beta.-acetyl-3.alpha.,12.alpha.-diacetoxy-5.beta.-androstane which in 13 steps was converted to 12.alpha.=(2,2-dimethylbutyryloxy)-3.alpha.-hydroxy-17.beta.-[2-(4R-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-on-6R-yl)ethyl]-5.beta.-androst-8(1H)-ene (II). In ex vivo test for antihypercholesterolemic activity, II at 3 mg/kg, p.o., inhibited 47% in HMG-CoA reductase screen.

MSTR 1D



G12 = SO2
MPL: claim 1
NTE: substitution is restricted

L15 ANSWER 28 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)

G31 = SH
G33 = C(O)
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: additional ring formation possible

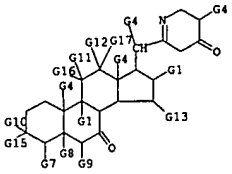
L15 ANSWER 30 OF 30 MARPAT COPYRIGHT 2003 ACS
ACCESSION NUMBER: 116:76355 MARPAT
TITLE: Glycoalkaloids for control of cell autophagy, cell agglutination, or immobilization of motile cells, and method for identifying suitable compounds
INVENTOR(S): Cham, Bill Elliott; Daunter, Brian
PATENT ASSIGNEE(S): Cura Nominees Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9110743	A1	19910725	WO 1991-AU20	19910118
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2073855	AA	19910719	CA 1991-2073855	19910118
AU 9171594	A1	19910805	AU 1991-71594	19910118
AU 654474	B2	19941110		
BR 9105952	A	19921117	BR 1991-5952	19910118
EP 515386	A1	19921202	EP 1991-901984	19910118
EP 515386	B1	19991222		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05503847	T2	19930624	JP 1991-502586	19910118
JP 3168542	B2	20010521		
AT 188036	E	20000115	AT 1991-901984	19910118
US 5958770	A	19990928	US 1996-743671	19961106
PRIORITY APPLN. INFO.:			AU 1990-8243	19900118
			WO 1991-AU20	19910118

AB Methods to control cellular autophagy, cellular agglutination, and the immobilization of motile cells and to identify agents to do so are disclosed. Such control is useful in, e.g., the treatment of cancer, contraception, termination of pregnancy, removal of pathogenic organisms, and removal of any abnormal cellular growth (malignant or otherwise); as a diagnostic and anal. tool whereby cell structure can be studied and testing could be undertaken for the presence (and subsequent anal.) of pathogenic and nonpathogenic organisms; and in the manuf. of biochems. whereby certain cells must be destroyed or otherwise contained. From surface anal. of normal and abnormal cells, specific receptors on abnormal cells which are either not present on normal cells or are only present in significantly reduced nos. can be identified. Alkaloids and other pharmaceutically acceptable compds. are preferentially recognized by the abnormal cells, and which bind thereto and subsequently destroy. The LD50 by solamargine against ovarian cancer cells was 6-40 times less than that of other cytotoxic agents studied (vinblastine, chlorambucil, cis-platinum).

MSTR 1C

L15 ANSWER 30 OF 30 MARPAT COPYRIGHT 2003 ACS (Continued)

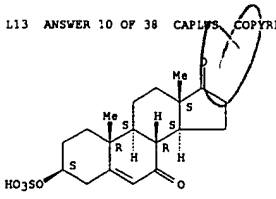


G10 = NH2
MPL: claim 12
NTE: carbohydrate selected from glycerose, erythrose, threose, ribose, arabinose, xylose, lyxose, altrose, allose, gulose, mannose, glucose, idose, galactose, talose, rhamnose, erthrulose, ribulose, xylulose, psicose, fructose, sorbose, tagatose, apiose, hamamelose, streptose, cordycepose, mycarose, and cladinose

```
=> d his

     (FILE 'HOME' ENTERED AT 13:47:14 ON 11 FEB 2003)

     FILE 'REGISTRY' ENTERED AT 13:47:20 ON 11 FEB 2003
L1                STRUCTURE UPLOADED
L2              1 S L1
L3                STRUCTURE UPLOADED
L4              5 S L3
L5            677 S L3 FULL
L6                STRUCTURE UPLOADED
L7            677 S L6 FULL SUB=L5
L8                STRUCTURE UPLOADED
L9            675 S L8 FULL SUB=L7
L10               STRUCTURE UPLOADED
L11            27 S L10 FULL SUB=L9

     FILE 'USPATFULL' ENTERED AT 14:00:50 ON 11 FEB 2003
L12             4 S L11

     FILE 'CAPLUS' ENTERED AT 14:02:32 ON 11 FEB 2003
L13            38 S L11

     FILE 'MARPAT' ENTERED AT 14:11:58 ON 11 FEB 2003
L14             2 S L11
L15            30 S L11 FULL

=> d his

     (FILE 'HOME' ENTERED AT 13:47:14 ON 11 FEB 2003)

     FILE 'REGISTRY' ENTERED AT 13:47:20 ON 11 FEB 2003
L1                STRUCTURE UPLOADED
L2              1 S L1
L3                STRUCTURE UPLOADED
L4              5 S L3
L5            677 S L3 FULL
L6                STRUCTURE UPLOADED
L7            677 S L6 FULL SUB=L5
L8                STRUCTURE UPLOADED
L9            675 S L8 FULL SUB=L7
L10               STRUCTURE UPLOADED
L11            27 S L10 FULL SUB=L9

     FILE 'USPATFULL' ENTERED AT 14:00:50 ON 11 FEB 2003
L12             4 S L11

     FILE 'CAPLUS' ENTERED AT 14:02:32 ON 11 FEB 2003
L13            38 S L11

     FILE 'MARPAT' ENTERED AT 14:11:58 ON 11 FEB 2003
L14             2 S L11
L15            30 S L11 FULL

     FILE 'BEILSTEIN' ENTERED AT 14:14:20 ON 11 FEB 2003
L16            30 S L10 FULL
```

FILE 'REGISTRY' ENTERED AT 14:15:21 ON 11 FEB 2003
SAVE L11 S128/A

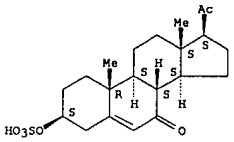
L13 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:514480 CAPLUS
DOCUMENT NUMBER: 131:269114
TITLE: Nano-electrospray tandem mass spectrometry for the analysis of neurosteroid sulphates
AUTHOR(S): Griffiths, William J.; Liu, Suya; Yang, Yang; Purdy, Robert H.; Sjovall, Jan
CORPORATE SOURCE: Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, S-17177, Swed.
SOURCE: Rapid Communications in Mass Spectrometry (1999), 13(15), 1595-1610
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neurosteroids are synthesized in the central and peripheral nervous system or are derived from peripheral sources, and act in the nervous system. In the present study the authors have evaluated the potential for using nano-electrospray (nano-ES) tandem mass spectrometry (MS/MS) for the structural anal. and detection of neurosteroids, in particular, steroid sulfates found in brain. Complete structural information can be obtained from 1 ng (3 pmol) of steroid sulfate, while fragment ions characteristic of the sulfate ester group can be obtained from only 3 pg (10 fmol) of sample. These values correspond to the expected quantities of steroid sulfates (e.g., pregnenolone sulfate) in about 100 mg and 300 .mu.g of brain, resp. Deuterated neurosteroid sulfates added to homogenized rat brain have been successfully analyzed by nano-ES-MS/MS at a level of 50 pg/mg of brain.
IT **159735-65-6**
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(nano-electrospray tandem mass spectrometry for anal. of neurosteroid sulfates in brain and their CID spectra)
RN 159735-65-6 CAPLUS
CN Pregn-5-ene-7,20-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

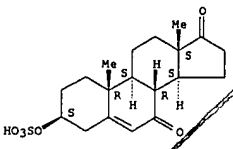
Absolute stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:96879 CAPLUS
DOCUMENT NUMBER: 130:276909
TITLE: Development and validation of a high-performance liquid chromatography assay for the quantitative determination of 7-oxo-dehydroepiandrosterone-3.beta.-sulfate in human plasma
AUTHOR(S): Marwah, Ashok; Marwah, Padma; Lardy, Henry
CORPORATE SOURCE: Institute for Enzyme Research, University of Wisconsin at Madison, Madison, WI, 53705, USA
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1999), 721(2), 197-205
CODEN: JCBBEF; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new, simple, reproducible and reliable high-performance liq. chromatog. method with UV absorbance detection at 240 nm was developed and validated for the detn. of 7-oxo-dehydroepiandrosterone-3.beta.-sulfate in human plasma. The method was based upon solid-phase (C18) extn. of plasma after addn. of 17.beta.-hydroxy-3.beta.-methoxyandrost-5-en-7-one as internal std. Using 1 mL of plasma for extn., the detection limit of the assay was 3 ng/mL. The std. curve was linear over the concn. range 10-1000 ng/mL. Stored at -20.degree.C for about 4 mo at various concns. in plasma, 7-oxo-dehydroepiandrosterone-3.beta.-sulfate did not reveal any appreciable degrdn. Also included herein is a method for the simultaneous detection and detn. of 7-oxo-dehydroepiandrosterone and 7-oxo-dehydroepiandrosterone-3.beta.-acetate in plasma.
IT **4121-96-4**
RL: ANT (Analyte); ANST (Analytical study)
(development and validation of a high-performance liq. chromatog. assay for the quant. detn. of 7-oxo-dehydroepiandrosterone-3.beta.-sulfate in human plasma)
RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

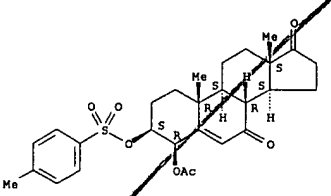
Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:598904 CAPLUS
DOCUMENT NUMBER: 130:81682
TITLE: Preparation of Androst-5-ene-4,7,17-trione and A-Norandrost-5-ene-3,7,17-trione
AUTHOR(S): Hanson, James R.; Kiran, Ismail; Masarweh, Natheer F.; Uyanik, Cavit
CORPORATE SOURCE: The School of Chemistry, The University of Sussex, Brighton, Sussex, BN1 9QJ, UK
SOURCE: Journal of Chemical Research, Synopses (1998), (9), 493, 2420-2434
CODEN: JRPSDC; ISSN: 0308-2342
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Syntheses are described of the aromatase inhibitor, androst-5-ene-4,7,17-trione, its 17.beta.-acetate, and A-nor analog, A-norandrost-5-ene-3,7,17-trione, starting from dehydroisoandrosterone and testosterone.
IT **75561-01-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of androst-5-ene-4,7,17-trione and A-norandrost-5-ene-3,7,17-trione)
RN 75561-01-2 CAPLUS
CN Androst-5-ene-7,17-dione, 4-(acetyloxy)-3-[[(4-methylphenyl)sulfonyl]oxy]-, (3.beta.,4.beta.)- (9CI) (CA INDEX NAME)

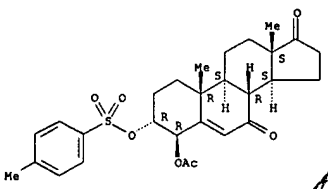
Absolute stereochemistry.



IT **218625-20-8P 218625-21-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of androst-5-ene-4,7,17-trione and A-norandrost-5-ene-3,7,17-trione)
RN 218625-20-8 CAPLUS
CN Androst-5-ene-7,17-dione, 4-(acetyloxy)-3-[[(4-methylphenyl)sulfonyl]oxy]-, (3.alpha.,4.beta.)- (9CI) (CA INDEX NAME)

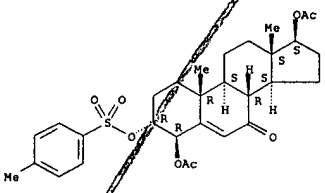
Absolute stereochemistry.

L13 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 218625-21-9 CAPLUS
CN Androst-5-en-7-one, 4,17-bis(acetyloxy)-3-[[(4-methylphenyl)sulfonyl]oxy]-, (3.alpha.,4.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

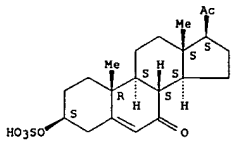
L13 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:6048 CAPLUS
DOCUMENT NUMBER: 128:110909
TITLE: Distinct sites for inverse modulation of N-methyl-D-aspartate receptors by sulfated steroids
AUTHOR(S): Park-Chung, Mijeong; Wu, Fong-Sen; Purdy, Robert H.; Malayev, Andrew A.; Gibbs, Terrell T.; Farb, David H.
CORPORATE SOURCE: Laboratory of Molecular Neurobiology, Department of Pharmacology, Boston University School of Medicine, Boston, MA, 02118, USA
SOURCE: Molecular Pharmacology (1997), 52(6), 1113-1123
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Steroid sulfation occurs in nervous tissue and endogenous sulfated steroids can act as pos. or neg. modulators of N-methyl-D-aspartate (NMDA) receptor function. In the current study, structure-activity relationships for sulfated steroids were examd. in voltage-clamped chick spinal cord and rat hippocampal neurons in culture and in Xenopus laevis oocytes expressing NR1100 and NR2A subunits. The ability of pregnenolone sulfate (a pos. modulator) and epipregnanolone sulfate (a neg. modulator) to compete with each another, as well as with other known classes of NMDA receptor modulators, was examd. The results show that steroid pos. and neg. modulators act at specific, extracellularly directed sites that are distinct from one another and from the spermine, redox, glycine, Mg2+, MK-801, and arachidonic acid sites. Sulfated steroids are effective as modulators of ongoing glutamate-mediated synaptic transmission, which is consistent with their possible role as endogenous neuromodulators in the CNS.

IT **159735-65-6**, 7-Ketopregnenolone sulfate
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(distinct sites for inverse modulation of N-methyl-D-aspartate receptors by sulfated steroids)

RN 159735-65-6 CAPLUS
CN Pregn-5-ene-7,20-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:637506 CAPLUS
DOCUMENT NUMBER: 126:6438
TITLE: Vaccine compositions and method for enhancing an immune response
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 34 pp., Cont-in-part of U. S. Ser. No. 13,972, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5562910	A	19961008	US 1993-123843	19930909
US 5827841	A	19981027	US 1994-295068	19940920
US 5753237	A	19980519	US 1994-309704	19940921
US 5919465	A	19990706	US 1994-309717	19940921
US 5837269	A	19981117	US 1995-487173	19950607

PRIORITY APPLN. INFO.: US 1989-412270 19890925
US 1991-779499 19911018
US 1993-13972 19930204
US 1993-18471 19930216
US 1993-123843 19930909
US 1994-219418 19940329

OTHER SOURCE(S): MARPAT 126:6438

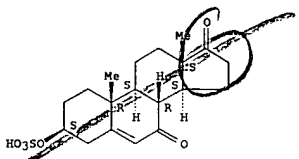
AB The invention relates to a vaccine which comprises an antigen and an immune response augmenting agent. The immune response augmenting agent is capable of enhancing T cell lymphokine prodn. Suitable immune response augmenting agents include, but are not limited to, dehydroepiandrosterone (DHEA) and DHEA-derivs. Examples of DHEA derivs. include DHEA-sulfate (DHEA-S), 16.alpha.-bromo-DHEA, 7-oxo-DHEA, 16.alpha.-bromo-DHEA-S and 7-oxo-DHEA-S. The invention also relates to a method for enhancing a vaccine-induced humoral immune response which comprises administering a vaccine which comprises an antigen and an immunomodulator. The immunomodulator may be an immune response augmenting agent, a lymphoid organ modifying agent or a mixt. of the immune response augmenting agent and lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include, but are not limited to, 1,25-dihydroxy Vitamin D3, biol. active Vitamin D3 derivs. which are capable of activating the intracellular Vitamin D3 receptor, all trans-retinoic acid, retinoic acid derivs., retinol, retinol derivs. and glucocorticoid. Alternatively, the method for enhancing a vaccine-induced humoral immune response comprises sep. administering the immunomodulator and a vaccine contg. an antigen.

IT **4121-96-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaccine comprises antigen and immunomodulator or lymphoid organ modifying agent)

RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



L13 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:366050 CAPLUS
DOCUMENT NUMBER: 125:41730
TITLE: Vaccine compositions and method for induction of mucosal immune response via systemic vaccination
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 13,972, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5518725	A	19960521	US 1993-123844	19930909
CA 2153794	AA	19940818	CA 1994-2153794	19940203
WO 9417823	A1	19940818	WO 1994-US1220	19940203
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9462348	A1	19940829	AU 1994-62348	19940203
AU 679215	B2	19970626		
EP 686042	A1	19951213	EP 1994-909530	19940203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 72404	A2	19960429	HU 1995-2105	19940203
JP 08508718	T2	19960917	JP 1994-518202	19940203
US 5827841	A	19981027	US 1994-295068	19940920
US 5753237	A	19980519	US 1994-309704	19940921
US 5919465	A	19990706	US 1994-309717	19940921
US 5824313	A	19981020	US 1995-480567	19950607
FI 9503608	A	19950919	FI 1995-3608	19950728
NO 9503049	A	19951003	NO 1995-3049	19950803

PRIORITY APPLN. INFO.: US 1989-412270 19890925
US 1991-779499 19911018
US 1993-13972 19930204
US 1993-18471 19930216
US 1993-123844 19930909
WO 1994-US1220 19940203
US 1994-219418 19940329

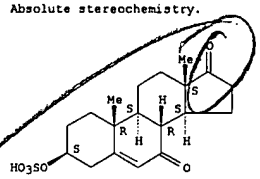
AB The invention relates to a vaccine which comprises an antigen and a lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include 1,25-dihydroxy Vitamin D3, biol. active Vitamin D3 derivs. which are capable of activating the intracellular Vitamin D3 receptor, all trans-retinoic acid, retinoic acid derivs., retinol, retinol derivs. and glucocorticoid. The vaccine compn. may further comprise an immune response augmenting agent which enhances T cell lymphokine prodn. Suitable immune response augmenting agents include dehydroepiandrosterone (DHEA) and DHEA-derivs. Examples of DHEA derivs. include DHEA-sulfate (DHEA-S), 16-.alpha.-bromo-DHEA, 7-oxo-DHEA, 16-.alpha.-Br-DHEA-S and 7-oxo-DHEA-S. The invention also relates to a method for inducing an antigen-specific mucosal immune response in a vertebrate animal which comprises administering a vaccine which comprises an antigen and a lymphoid organ modifying agent with or without an immune response

L13 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)
augmenting agent to a site which drains into a peripheral lymphoid compartment.

IT **4121-96-4**, 7-Oxo-5,6-dehydroepiandrosterone sulfate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaccine compns. and method for induction of mucosal immune response via systemic vaccination)

RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



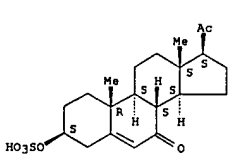
L13 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:247978 CAPLUS
DOCUMENT NUMBER: 122:23982
TITLE: Steroid potentiation and inhibition of N-methyl-D-aspartate receptor-mediated intracellular Ca++ responses: structure-activity studies
AUTHOR(S): Irwin, Robert P.; Lin, Sui-Zhen; Rogawski, Michael A.; Purdy, Robert H.; Paul, Steven M.
CORPORATE SOURCE: Section Mol. Pharmacol., Natl. Inst. Neurol. Disorders Stroke, Bethesda, MD, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1994), 271(2), 677-82
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pregnenolone sulfate and 15 related steroids were investigated for their effects on N-methyl-D-aspartate (NMDA)-induced elevations in intracellular Ca++ ([Ca++]i) in cultured rat hippocampal neurons by microspectrofluorimetry with the Ca++-sensitive indicator fura-2. Several pregn-5-ene steroids markedly potentiated NMDA-mediated [Ca++]i responses. Pregnenolone sulfate and its 21-acetoxy deriv. and pregnenolone hemisuccinate were the most active. At a concn. of 50 .mu.M, each produced approx. 300% potentiation of 5 .mu.M NMDA responses. In addn., several steroids were identified that inhibited NMDA-induced elevations in [Ca++]i, the most potent of which was 3.alpha.-hydroxy-5.beta.-pregnan-20-one sulfate (IC50, 37 .mu.M). Concn.-response curves for NMDA in the presence of active steroids revealed noncompetitive interaction(s) of these steroids with the NMDA receptor. Although the mechanism(s) responsible for either steroid-induced augmentation or inhibition of NMDA-receptor responses is unknown, these data suggest the presence of one or more steroid recognition sites with a high degree of structural specificity assocd. with NMDA receptors. These results further raise the possibility that pregn-5-ene 3-sulfates and pregnane 3-sulfates could be endogenous modulators of NMDA receptor-mediated synaptic events.

IT **159735-65-6**, 7-Ketopregnenolone sulfate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure-activity of steroid potentiation and inhibition of NMDA receptor-mediated intracellular hippocampal neuron calcium responses)

RN 159735-65-6 CAPLUS
CN Pregn-5-ene-7,20-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



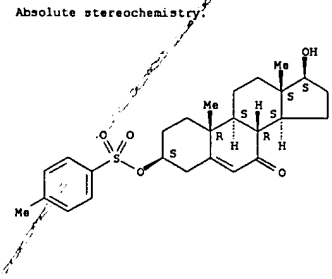
L13 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:534550 CAPLUS
DOCUMENT NUMBER: 121:134550
TITLE: Synthesis of Androst-5-en-7-ones and Androsta-3,5-dien-7-ones and Their Related 7-Deoxy Analogs as Conformational and Catalytic Probes for the Active Site of Aromatase
AUTHOR(S): Numazawa, Mitsuteru; Mutsumi, Ayako; Tachibana, Mii; Hoshi, Kumiko
CORPORATE SOURCE: Tohoku College of Pharmacy, Sendai, 981, Japan
SOURCE: Journal of Medicinal Chemistry (1994), 37(14), 2198-205
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of androst-5-en-7-ones and androsta-3,5-dien-7-ones and their 7-deoxy derivs., resp., were synthesized and tested for their abilities to inhibit aromatase in human placental microsomes. All the steroids inhibited the enzyme in a competitive manner with Ki's ranging from 0.058 to 45 .mu.M. The inhibitory activities of 17-oxo compds. were much more potent than those of the corresponding 17.beta.-alcs. in each series. Steroids having an oxygen function (hydroxy or carbonyl) at C-19 were less potent inhibitors than the corresponding compds. having a 19-Me group. 3,5-Dien-7-one I [X = O, R = Me, CHO, CH2OH, R1R2 = bond] as well as I [X = O, R = CHO, R1, R2 = H] caused a time-dependent inactivation of aromatase only in the presence of NADPH in which the kinact values of I [R = CHO] (0.143 and 0.189 min-1, resp.) were larger than those of I [R = Me, CH2OH]. I [X = O, R-R2 = H], but not I [X = O, R = H, R1R2 = bond] also inactivated the enzyme in a time-dependent manner. In contrast, I [X = H2, R = Me, R1R2 = H2, bond] did not cause enzyme inactivation. The inactivations were prevented by the substrate androstenedione, and no significant effects of L-cysteine on the inactivations were obsd. in each case. The results suggest that oxygenation at C-19 would be at least in part involved in the inactivations caused by the inhibitors I [X = O, R = Me, R1R2 = H2, bond]. The conjugated enone structures should play a crit. role in the inactivation sequences.

IT **157022-85-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of; in prepn. of aromatase inhibitors)

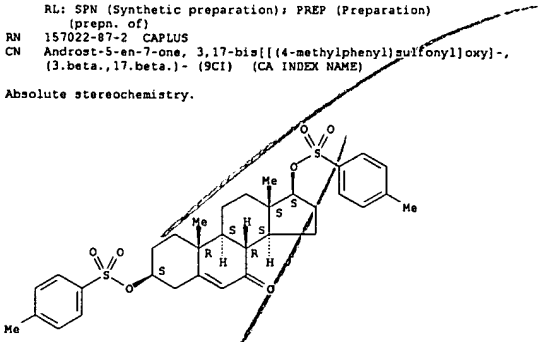
RN 157022-85-0 CAPLUS
CN Androst-5-en-7-one, 17-hydroxy-3-[[(4-methylphenyl)sulfonyl]oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



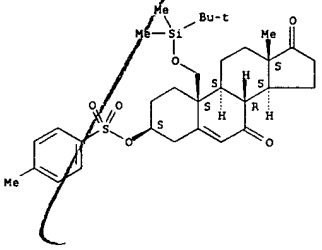
L13 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)
IT **157022-87-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 157022-87-2 CAPLUS
CN Androst-5-en-7-one, 3,17-bis[[(4-methylphenyl)sulfonyl]oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



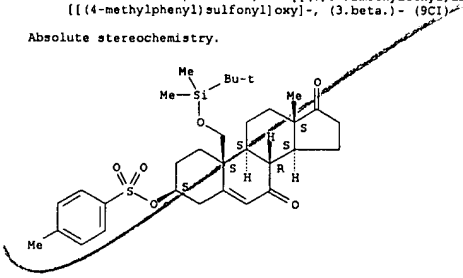
IT **145724-07-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of aromatase inhibitors)
RN 145724-07-8 CAPLUS
CN Androst-5-ene-7,17-dione, 19-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[[(4-methylphenyl)sulfonyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



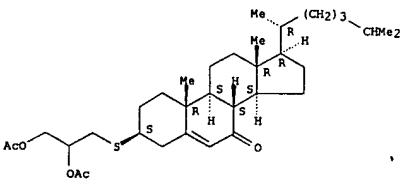
L13 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:75905 CAPLUS
DOCUMENT NUMBER: 118:75905
TITLE: Androst-5-ene-7,17-dione: a novel class of suicide substrate of aromatase
AUTHOR(S): Numazawa, Mitsuteru; Mutsumi, Ayako; Hoshi, Kumiko; Tanaka, Yuko
CORPORATE SOURCE: Tohoku Coll. Pharm., Sendai, 981, Japan
SOURCE: Biochemical and Biophysical Research Communications (1992), 186(1), 32-9
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Androst-5-ene-7,17-dione (I) was found to be a potent inhibitor of aromatase. This along with its 19-hydroxy deriv. (II) was characterized as suicide substrate of human placental aromatase (kinact values of 0.069 and 0.058 min-1 and Ki values of 143 nM and 11.1 .mu.M, resp., for steroids I and II). The results suggested that the 19-oxygenation would be involved in the irreversible inactivation of aromatase by the 5-en-7-one steroids.
IT **145724-07-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deprotection of)
RN 145724-07-8 CAPLUS
CN Androst-5-ene-7,17-dione, 19-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[[(4-methylphenyl)sulfonyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:185838 CAPLUS
DOCUMENT NUMBER: 114:185838
TITLE: Reaction of 1-thioglycerol with some 3-substituted cholest-5-en-7-ones
AUTHOR(S): Shafiullah; Shamsuzzaman; Khan, Badiuzzaman; Ahmad, Suhail
CORPORATE SOURCE: Dep. Chem., Aligarh Muslim Univ., Aligarh, 202 002, India
SOURCE: Acta Chimica Hungarica (1990), 127(5), 705-10
CODEN: ACHUDC; ISSN: 0231-3146
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:185838
AB 3.beta.-Chloro-5-cholesten-7-one on treatment with HSCH2CH(OH)CH2OH in the presence of BF3.OEt2 in HOAc afforded the oxathiane I [R = CH2CH(OAc)CH2SH] in addn. to the enones II [R = OCH2CH(OAc)CH2SH (III), OCH2CH(OH)CH2SAc, SCH2CH(OAc)CH2OH, OCH(CH2OH)CH2SAc]. Similar treatment of 3.beta.-acetoxy-5-cholesten-7-one gave III and II [R = SCH2CH(OH)CH2OAc]. Diacetates II [R = OCH2CH(OAc)CH2SAc, SCH2CH(OAc)CH2OAc, CH(CH2OAc)CH2SAc] were prepd. by acetylation of the appropriate precursors. Structures of the prepd. compds were detd. by anal. and spectral data.
IT **133337-97-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 133337-97-0 CAPLUS
CN Cholest-5-en-7-one, 3-[[2,3-bis(acetyloxy)propyl]thio]-, (3.beta.)- (9CI) (CA INDEX NAME)

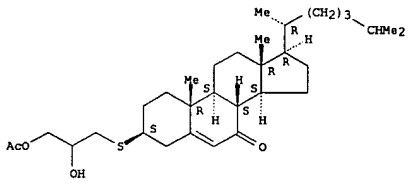
Absolute stereochemistry.



IT **133337-99-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, by reaction of thioglycerol and cholestenones)
RN 133337-99-2 CAPLUS
CN Cholest-5-en-7-one, 3-[[3-(acetyloxy)-2-hydroxypropyl]thio]-, (3.beta.)- (9CI) (CA INDEX NAME)

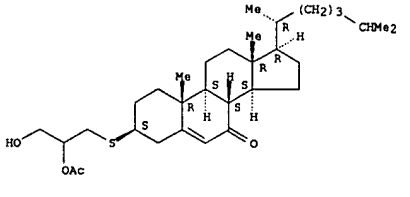
Absolute stereochemistry.

L13 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



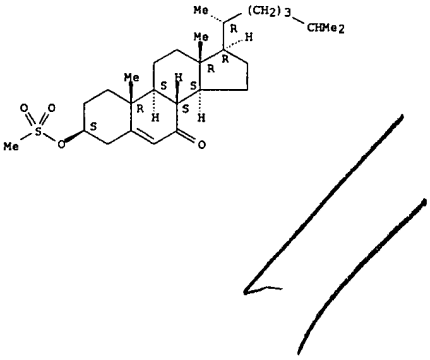
IT **133337-94-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, by reaction. of thioglycerol and cholestenones)
RN 133337-94-7 CAPLUS
CN Cholest-5-en-7-one, 3-[[2-(acetyloxy)-3-hydroxypropyl]thio]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



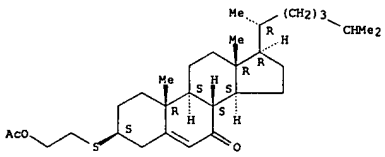
L13 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:560765 CAPLUS
DOCUMENT NUMBER: 103:160765
TITLE: Synthesis of some allylic acetoxy derivatives in the steroid series
AUTHOR(S): Stary, Ivo; Kocovsky, Pavel
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10/6, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications (1985), 50(5), 1227-38
CODEN: CCCCAK; ISSN: 0366-547X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 103:160765
AB Diacetoxycholest-1-ene I, diastereoisomeric diacetoxycholest-5-enes II, and epimeric triacetoxycholest-5-enes III were prepd. E.g., treatment of 19-acetoxy-5.alpha.-cholestan-3-one with trimethylanilinium hydrobromide perbromide in THF gave the C-2.alpha.-bromo deriv., which underwent dehydrobromination, LiAlH4 redn., and acetylation to give I. 3.alpha.-Substituted cholest-5-enes were prepd. via reductive ring cleavage of 3.alpha.,4.alpha.-epoxycholest-5-en-7-one.
IT **80108-85-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and acetolysis of)
RN 80108-85-6 CAPLUS
CN Cholest-5-en-7-one, 3-[(methylsulfonyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1984:511261 CAPLUS
DOCUMENT NUMBER: 101:111261
TITLE: Reaction of .beta.-mercaptoethanol with .alpha.,.beta.-unsaturated steroidal ketones: synthesis of steroidal thioethers
AUTHOR(S): Shafiullah; Shamsuzzaman; Khan, B. Z.
CORPORATE SOURCE: Dep. Chem., Aligarh Muslim Univ., Aligarh, 202 001, India
SOURCE: Journal of the Indian Chemical Society (1983), 60(11), 1109-10
CODEN: JICSAH; ISSN: 0019-4522
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment of 3.beta.-acetoxycholest-5-en-7-one with HSCH2CH2OH in HOAc contg. F3B.OEt2 gave 32% 3.beta.-acetoxy-4.alpha.-[(2-acetoxyethyl)thio]cholest-5-en-7-one, 23% 3.beta.-[(2-acetoxyethyl)thio]cholest-5-en-7-one (I), 15% 3.alpha.-[(2-acetoxyethyl)thio]cholest-5-en-7-one (II), 8% 4.alpha.-[(2-acetoxyethyl)thio]cholest-5-en-7-one (III), and 5% 4.alpha.-[(2-hydroxyethyl)thio]cholest-5-en-7-one (IV). Similar treatment of 3.beta.-chlorocholest-5-en-7-one gave 38% I, 28% II, 7% III, and 4% IV.
IT **80239-89-0P 80239-90-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 80239-89-0 CAPLUS
CN Cholest-5-en-7-one, 3-[[2-(acetyloxy)ethyl]thio]-, (3.beta.)- (9CI) (CA INDEX NAME)

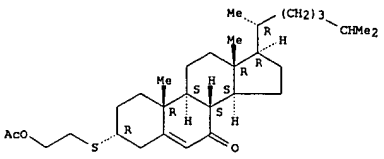
Absolute stereochemistry.



RN 80239-90-3 CAPLUS
CN Cholest-5-en-7-one, 3-[[2-(acetyloxy)ethyl]thio]-, (3.alpha.)- (9CI) (CA INDEX NAME)

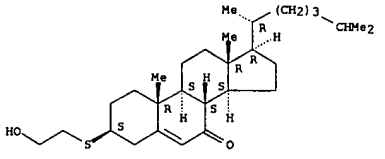
Absolute stereochemistry.

L13 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)



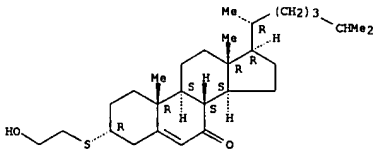
L13 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:20366 CAPLUS
DOCUMENT NUMBER: 96:20366
TITLE: Synthesis of steroidal thio ethers
AUTHOR(S): Shafiullah; Shamsuzzaman; Ali, Hasrat; Ghaffari, M. A.
CORPORATE SOURCE: Steroid Res. Lab., Aligarh Muslim Univ., Aligarh, 202001, India
SOURCE: Synthetic Communications (1981), 11(9), 751-6
CODEN: SYNCAV; ISSN: 0039-7911
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Substitution reactions of cholestenones I (R = AcO, Cl; R1 = H) with HOCH2CH2SH gave I (R = HOCH2CH2S, R1 = H; R = H, R1 = HOCH2CH2S), which were acetylated to give I (R = AcOCH2CH2S, R1 = H; R = H, R1 = AcOCH2CH2S).
IT **80239-87-8P 80239-88-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and acetylation of)
RN 80239-87-8 CAPLUS
CN Cholest-5-en-7-one, 3-[(2-hydroxyethyl)thio]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 80239-88-9 CAPLUS
CN Cholest-5-en-7-one, 3-[(2-hydroxyethyl)thio]-, (3.alpha.)- (9CI) (CA INDEX NAME)

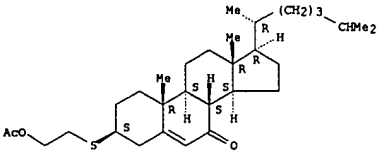
Absolute stereochemistry.



IT **80239-89-0P 80239-90-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 80239-89-0 CAPLUS

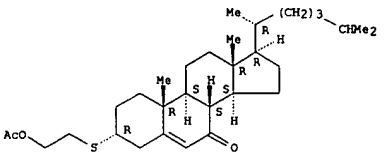
L13 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN Cholest-5-en-7-one, 3-[[2-(acetyloxy)ethyl]thio]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



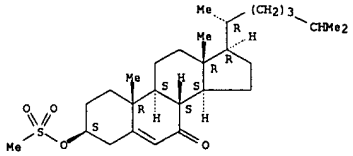
RN 80239-90-3 CAPLUS
CN Cholest-5-en-7-one, 3-[[2-(acetyloxy)ethyl]thio]-, (3.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



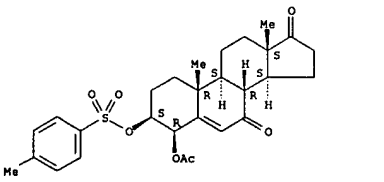
L13 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:20362 CAPLUS
DOCUMENT NUMBER: 96:20362
TITLE: Steroids. CCXLVII. Synthesis of 5,6-cyclopropanocholestane derivatives with an oxygen function in position 7
AUTHOR(S): Kohout, Ladislav
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Czechoslovak Acad. Sci., Prague, 166 10, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications (1981), 46(8), 1828-38
CODEN: CCCCAK; ISSN: 0366-547X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Simmons-Smith methylenation of cholest-5-en-7.beta.-ol gave 5.beta.,6.beta.-cyclopropanocholestanol I (R = HO, R1 = H), which was oxidized to give I (RR1 = O). LiAlH4 redn. of I (RR1 = O) gave epimeric I (R = H, R1 = HO). Analogous treatment of cholest-5-en-7.alpha.-ol gave 5.alpha.,6.alpha.-cyclopropanocholestanes II (R2 = H, R3 = HO; R2R3 = O; R2 = HO, R3 = H).
IT **80108-85-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 80108-85-6 CAPLUS
CN Cholest-5-en-7-one, 3-[(methylsulfonyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



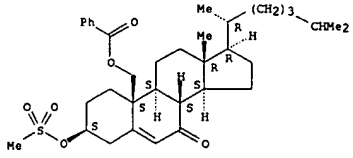
L13 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1980:620970 CAPLUS
DOCUMENT NUMBER: 93:220970
TITLE: The solvolysis of 4.beta.-hydroxy-3.beta.-p-tolylsulfonyloxyandrost-5-enes
AUTHOR(S): Hanson, James R.; Wadsworth, Harry J.
CORPORATE SOURCE: Sch. Mol. Sci., Univ. Sussex, Brighton, BN1 9QJ, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1980), (4), 933-7
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The rates of solvolysis of steroids I (R = OAc, R1 = R2 = H, R1R2 = O; R = OH, R1 = R2 = H) and steroids II (R = OH, OAc) in NaOAc/AcOH, compared with those of I (R = R1 = R2 = H) and II (R = H), were retarded by the 4.beta.-hydroxy or 4.beta.-acetoxy group. The products of solvolysis include the 3.beta.-formyl A-norsteroids, except in the presence of a 7-ketone.
IT **75561-01-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidn. and kinetics of acetolysis of)
RN 75561-01-2 CAPLUS
CN Androst-5-ene-7,17-dione, 4-(acetyloxy)-3-[[(4-methylphenyl)sulfonyl]oxy]-, (3.beta.,4.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:510109 CAPLUS
DOCUMENT NUMBER: 89:110109
TITLE: Steroids; Part CCIV. 19-Norsteroids substituted in position 7
AUTHOR(S): Fajkos, Jan; Joska, Jiri
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications (1978), 43(4), 1142-51
CODEN: CCCCAK; ISSN: 0366-547X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The redn. of 5-bromo-6.beta.,19-epoxy-5.alpha.-cholestan-3.beta.-yl benzoate using Zn-AcOH followed by acetylation, H2CrO4 oxidn., partial hydrolysis, and oxidn. with Jones reagent gave 3.beta.-benzoyloxy-7-oxocholest-5-en-19-oic acid (I). The decarboxylation of I gave norcholestadienone II, which also was prepd. from cholest-5-ene-3.beta.,19-diyl 3-acetate 19-benzoate by oxidn., partial hydrolysis, mesylation, demesyloxylation, debenzoylation, oxidn. by Jones reagent, and decarboxylation. Hydride redn. of 7-oxocholest-5-ene-3,19-diyl-3-acetate 19-benzoate with successive benzoylation, deacetylation, oxidn. with Al(OCHMe2)3, hydrolysis-dehydration, and oxidn. with Jones reagent gave 3-oxocholesta-4,6-dien-19-oic acid which was decarboxylated to give norcholestadienone III.
IT **67308-59-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and in hydride redn. of)
RN 67308-59-2 CAPLUS
CN Cholest-5-en-7-one, 19-(benzoyloxy)-3-[(methylsulfonyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib ab fqhit 1-10

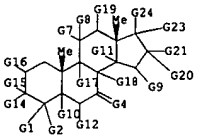
L6 ANSWER 1 OF 10 MARPAT COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:129430 MARPAT
TITLE: Preparation of meiosis regulating compounds for use as contraceptives or compounds to treat infertility
INVENTOR(S): Gronvald, Frederick Christian; Faarup, Peter; Guddal, Erling
PATENT ASSIGNEE(S): Den.
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 436,810, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002013302	A1	20020131	US 2001-878884	20010611
WO 9700884	A1	19970109	WO 1996-DK273	19960621
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
ZA 9605333	A	19970123	ZA 1996-5333	19960624
PRIORITY APPLN. INFO.:			DK 1995-728	19950623
			DK 1995-730	19950623
			DK 1995-1461	19951222
			WO 1996-DK273	19960621
			US 1997-973661	19971219
			US 1999-436810	19991109

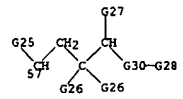
AB Sterol deriv. compds., structurally related to natural compds. which can be extd. from bull testes and from human follicular fluid, useful for regulating meiosis in oocytes and in male germ cells. Some of these compds. are useful in the treatment of infertility, whereas other compds. are useful as contraceptives.

MSTR 1E



G4 = O
G14 = OH
G24 = 57

L6 ANSWER 1 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)



G25 = alkyl<(1-4)>
G30 = Ak<EC (1-) C, BD (ALL) SE> (SO G31)
MPL: claim 1
NTE: additional methylene, oxo, hydroximino, ring, and double bond formation also claimed
NTE: substitution is restricted

L6 ANSWER 2 OF 10 MARPAT COPYRIGHT 2002 ACS

ACCESSION NUMBER: 133:350394 MARPAT
TITLE: Preparation of steroid derivatives
INVENTOR(S): Liao, Shutsung; Song, Ching
PATENT ASSIGNEE(S): Arch Development Corporation, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

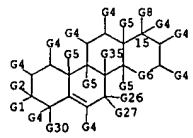
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066611	A1	20001109	WO 2000-US11243	20000427
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1189922	A1	20020327	EP 2000-928431	20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010197	A	20020716	BR 2000-10197	20000427
NO 2001005314	A	20011227	NO 2001-5314	20011030
PRIORITY APPLN. INFO.:			US 1999-131728P	19990430
			US 2000-191864P	20000324
			WO 2000-US11243	20000427

AB The steroid derivs. I (R3 = H, amino, carboxyl, oxo, halo, sulfonic acid, -O-sulfonic acid, or alkyl that is optionally inserted with -NH-,-N(alkyl)-, -O-, -S-, -SO-, -SO2-, -O-SO2-, -SO2-O-, -O-SO3-, -SO3-O-, -CO-, -CO-O-, -O-CO-, -CO-NH-, -CO-N(alkyl)-, -NH-CO-, or -N(alkyl)-CO-, and further optionally substituted with hydroxy, halo, amino, carboxyl, sulfonic acid, or -O-sulfonic acid),. R1, R2, R4, R4', R6, R7, R11, R12, R15, R16, and R17', independently, is H, hydroxy, amino, carboxyl, oxo, halo, sulfoic acid, -O-sulfonic acid, or alkyl that is optionally inserted with -NH-, -N(alkyl)-, -O-, -S-, -SO-, -SO2-, -O-SO2-, -SO2-O-, -O-SO3-, -SO3-O-, -CO-, -CO-O-, -O-CO-, -CO-NH-, -CO-N(alkyl)-, -NH-CO-, or -N(alkyl)-CO-, and further optionally substituted with hydroxy, halo, amino, carboxyl, sulfonic acid, or -O-sulfonic acid. R5, R8, R9, R10, R13, and R14, independently, is H, alkyl, haloalkyl, hydroxyalkyl, alkoxy, hydroxy, or amino; R17 is -X-Y-Z, in which X is a bond, or alkyl or alkenyl, optionally inserted with -NH-, -N(alkyl)-, -O-, or -S-, and further optionally forming a cyclic moiety with R16 and the 2 ring carbon atoms to which R16 and R17 are bonded; Y is -CO-, -SO-, -SO2-, -O-SO2-, -SO2-O-, -O-SO3-, -SO3-O-, -CO-O-, -O-CO-, -CO-NH-,-CO-N(alkyl)-, -NH-CO-, -N(alkyl)-CO-, or a bond. Z = alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, aralkyl, or heteroaralkyl, and is optionally substituted with hydroxy, alkoxy, amino, halo, sulfonic acid, -O-sulfonic acid, carboxyl, oxo, alkyloxycarbonyl, alkylcarbonyloxy, alkylaminocarbonyl, alkylcarbonylamino, alkylcarbonyl, alkylsulfinyl, alkylsulfonyl, or alkylthio; or is -CH(A)-B with A being a side chain of an amino acid, and B being hydrogen, -NRaRb, or -COORc wherein each of Ra, Rb, and Rc, independently, is hydrogen or alkyl; n is 0, 1, or 2. Provided that when Z is substituted with carboxyl or alkyloxycarbonyl, Y is a bond and either X or Z contains at least one double bond, and that when Y is a bond,

L6 ANSWER 2 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)

either X is -NH-alkyl, -NH-alkenyl, -N(alkyl)-alkyl-, -N(alkyl)-alkenyl-, -O-alkyl-, -O-alkenyl-, -S-alkyl-, or -S-alkenyl-; or Z is substituted with halo, sulfonic acid, -O-sulfonic acid, alkylsulfinyl, or alkylsulfonyl, or is alkenyl or their salts were prepd. Thus, to a stirred soln. of L- (or D-) phenylalanine ester hydrochloride in dry DMF was added triethylamine and the mixt. was stirred at room temp. for 10 min, bile acid and 1-ethyl-3-[3-dimethylaminopropyl]-carbodiimide were then added and the suspension was stirred at room temp. overnight. Reaction mixt. was dild. with water and Et acetate, the org. layer was sepd. and the water layer was extd. with Et acetate again, the combined org. layer was then washed with 1N HCl, water, 1N NaOH and water, and dried (MgSO4), removed the solvent under reduced pressure to afford the steroid derivs., e.g. II. Steroid derivs. of I interact with nuclear liver X receptor (LXR) and ubiquitous receptor (UR), and can be used to treat a variety of LXR- or UR- mediated disorders.

MSTR 1C



G1 = OH
G17 = alkylene<(1-8)>
G26+G27= O
MPL: claim 1
NTE: additional derivatization also claimed
NTE: substitution is restricted
NTE: or salts
NTE: also incorporates claims 18, 35 and 49

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

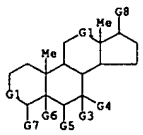
L6 ANSWER 3 OF 10 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 130:76173 MARPAT
TITLE: Method using dehydroepiandrosterone derivative for reducing mast cell-mediated allergic reactions
INVENTOR(S): Dowell, Tad; Norton, Steven D.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA; Pharmadigm, Inc.
SOURCE: U.S., 20 pp., Cont.-in-part of U.S. Ser. No. 870,234.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5859000	A	19990112	US 1997-966385	19971107
US 5811418	A	19980922	US 1995-480747	19950607
US 5846963	A	19981208	US 1995-516540	19950818
US 5753640	A	19980519	US 1995-580716	19951229
US 5977095	A	19991102	US 1997-870234	19970605
CA 2308406	AA	19990520	CA 1998-2308406	19981030
WO 9924039	A1	19990520	WO 1998-US23038	19981030
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9912895	A1	19990531	AU 1999-12895	19981030
AU 736614	B2	20010802		
EP 1033989	A1	20000913	EP 1998-956356	19981030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001522803	T2	20011120	JP 2000-520131	19981030

PRIORITY APPLN. INFO.: US 1995-480747 19950607
US 1995-516540 19950818
US 1995-580716 19951229
US 1997-870234 19970605
US 1993-29422 19930309
US 1994-284688 19940809
US 1995-480744 19950607
US 1995-480745 19950607
US 1995-480748 19950607
US 1997-966385 19971107
WO 1998-US23038 19981030

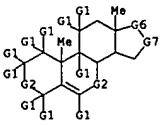
AB A method is provided for reducing mast cell-mediated allergic reactions, including mast cell-mediated allergy and asthma. Mast cell-mediated allergic reactions, including type I hypersensitivity response to allergens and asthma, are reduced by administering a dehydroepiandrosterone deriv. to a patient in a manner which quickly raises blood levels of the active agent.

MSTR 1



G1 = 23

L6 ANSWER 3 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)



G2 = 32 / C(O)

G3 = OH
G6 = 64

G7 = 97

G8 = alkyl<(1-10)>
DER: or pharmaceutically acceptable monosaccharides, disaccharides or oligosaccharides derivatives
MPL: claim 1
NTE: substitution is restricted
NTE: additional ring formation also claimed

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 10 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 130:43296 MARPAT
TITLE: Immunomodulating, bile-derivable compositions for the treatment of viral disorders
INVENTOR(S): Percheson, Paul
PATENT ASSIGNEE(S): Imutec Pharma Inc., Can.
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

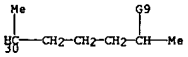
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9852585	A1	19981126	WO 1998-CA494	19980522
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2238460	AA	19981123	CA 1998-2238460	19980522
AU 9875160	A1	19981211	AU 1998-75160	19980522
ZA 9806224	A	19990429	ZA 1998-6224	19980713

PRIORITY APPLN. INFO.: CA 1997-2206047 19970523
WO 1998-CA494 19980522

AB The present invention relates to the use of a compn. exhibiting antiviral properties, comprising small mol. wt. components of less than 3000 daltons, and having the following properties: (a) is extractable from bile of animals; (b) is capable of stimulating monocytes and macrophages in vitro and in vivo; (c) is capable of modulating tumor necrosis factor prodn.; (d) contains no measurable IL-1.alpha., IL-1.beta., TNF, IL-6, IL-8, IL-4, GM-CSF or IFN-.gamma.; (e) shows no cytotoxicity to human peripheral blood mononuclear cells or lymphocytes; and (f) is not an endotoxin. The invention also relates to the use of the antiviral compn. when used in conjunction with other drugs such as antiviral compds. or immunomodulators such as interferon.

MSTR 1

L6 ANSWER 4 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)
G2 = OH
G8 = 30



G9 = Me
G3 +G4 = O
MPL: claim 23

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 10 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 128:154276 MARPAT
TITLE: Preparation of 6,7-oxygenated steroids and therapeutic uses related thereto
INVENTOR(S): Burgoyne, David L.; Shen, Yaping; Langlands, John M.; Rogers, Christine; Chau, Joseph H-L.; Piers, Edward; Salari, Hassan
PATENT ASSIGNEE(S): Inflazyme Pharmaceuticals Ltd., Can.
SOURCE: PCT Int. Appl., 236 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

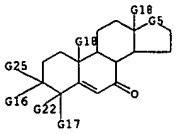
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9802450	A2	19980122	WO 1997-CA490	19970711
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6046185	A	20000404	US 1997-893575	19970710
CA 2259981	AA	19980122	CA 1997-2259981	19970711
AU 9733323	A1	19980209	AU 1997-33323	19970711
AU 722815	B2	20000810		
EP 917534	A2	19990526	EP 1997-929071	19970711
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1222159	A	19990707	CN 1997-195531	19970711
BR 9710353	A	20000111	BR 1997-10353	19970711
JP 2001503732	T2	20010321	JP 1997-535644	19970711
KR 2000023661	A	20000425	KR 1999-700116	19990109

PRIORITY APPLN. INFO.: US 1996-23450P 19960711
US 1996-679642 19960712
WO 1997-CA490 19970711

AB Steroid compds. of formula I [R = H, protecting group; positions C1-C17 independently substituted] having various oxygen substitution on the steroid nucleus are disclosed. Steroids having 3,4-epoxy functionality are also disclosed. In addn., steroids having C17 pyran and .delta.-lactone functionality, with oxygen substitution at C6 and C7, or at C15, of the steroid nucleus, are disclosed. Thus, II is prepd. from 4-androsten-3,17-dione in many steps. II showed antithrombolytic, antiallergic and antiasthmatic activity.

MSTR 3

L6 ANSWER 5 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)



G5 = 32

G7 = hydrocarbyl<(1-30)>
G16 = OH
DER: and pharmaceutically acceptable salts and solvates
MPL: claim 79
NTE: additional bond and ring formation, and substitution also claimed
NTE: substitution is restricted

L6 ANSWER 6 OF 10 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 124:146587 MARPAT
TITLE: Oxidation of steroids having allylic groups
INVENTOR(S): Miller, Ross A.; Thompson, Andrew S.; Bakshi, Raman K.; Corley, Edward G.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

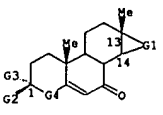
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532215	A1	19951130	WO 1995-US6004	19950515
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2190500	AA	19951130	CA 1995-2190500	19950515
AU 9525885	A1	19951218	AU 1995-25885	19950515
AU 688513	B2	19980312		
EP 759929	A1	19970305	EP 1995-920434	19950515
EP 759929	B1	20000823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 75778	A2	19970528	HU 1996-3187	19950515
CN 1152316	A	19970618	CN 1995-194043	19950515
BR 9507663	A	19971007	BR 1995-7663	19950515
JP 10500682	T2	19980120	JP 1995-530344	19950515
RU 2149875	C1	20000527	RU 1996-124063	19950515
AT 195741	E	20000915	AT 1995-920434	19950515
ES 2149365	T3	20001101	ES 1995-920434	19950515
RO 116550	B1	20010330	RO 1996-2171	19950515
SK 282278	B6	20020107	SK 1996-1478	19950515
US 6369247	B1	20020409	US 1996-718408	19960930
FI 9604610	A	19961118	FI 1996-4610	19961118

PRIORITY APPLN. INFO.: US 1994-245935 19940519
WO 1995-US6004 19950515

OTHER SOURCE(S): CASREACT 124:146587

AB A process for oxidizing .DELTA.5-steroidal alkenes contg. an allylic group to the corresponding enones, using a ruthenium-based catalyst in the presence of a hydroperoxide. Thus, cholesteryl acetate was oxidized by Me3COOH in presence of RuW11O39SiNa5 to the 7-oxo deriv. which was converted to 4,7.beta.-dimethyl-4-aza-5.alpha.-cholestan-3-one in 7 steps.

MSTR 2

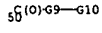


G1 = 20-13 22-14

L6 ANSWER 6 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)

G2 = OH (SO)
G4 = CH2
G6 = 72

G12 = alkyl<(1-10)> (SR 50)



MPL: claim 16

L6 ANSWER 7 OF 10 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 122:274034 MARPAT
TITLE: Immunomodulating compositions from bile
INVENTOR(S): Rang, Romeo
PATENT ASSIGNEE(S): Imutec Corp., Can.
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

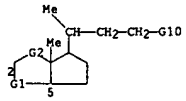
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9507089	A1	19950316	WO 1994-CA494	19940909
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2171281	AA	19950316	CA 1994-2171281	19940909
AU 9476489	A1	19950327	AU 1994-76489	19940909
EP 717631	A1	19960626	EP 1994-926737	19940909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1136777	A	19961127	CN 1994-194002	19940909
JP 09502706	T2	19970318	JP 1994-508370	19940909
NO 9600907	A	19960430	NO 1996-907	19960306
FI 9601109	A	19960506	FI 1996-1109	19960308
AU 9897242	A1	19990304	AU 1998-97242	19981221
AU 732816	B2	20010503		

PRIORITY APPLN. INFO.: US 1993-118269 19930909
US 1993-155303 19931122
US 1994-231726 19940424
AU 1994-76489 19940909
WO 1994-CA494 19940909

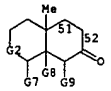
AB A compn. for use as an immunomodulator comprises small-mol.-wt. components (<3000 Da) extractable from bile of animals which (a) are capable of stimulating monocytes and macrophages in vitro; (b) are capable of modulating tumor necrosis factor prodn.; (c) contain no measurable IL-1a, IL-1b, TNF, IL-6, IL-8, IL-4, GM-CSF or IFN-.gamma.; (d) have an anti-proliferative effect in a malignant mouse hybridoma cell line; (e) show no cytotoxicity to human peripheral blood mononuclear cells; and (f) contain no endotoxin. The bile components may include steroids [I; X = H, OH, :O, OSO3H; Y = CHMe(CH2)3R1, CHMe(CH2)2R2; R1 = CHMe2, CHMeCH2OH, CHMeCHO, CO2H; R2 = CH(OH)CHMeCO2H, CO2H, CONHR; R = amino acid residue] and their .DELTA.4, .DELTA.5(6), and .DELTA.6 dehydro derivs., phospholipids, sphingolipids, diglycerides, oligosaccharides, mucin or proteoglycan hydrolysis products, fat-sol. vitamins, glutamic acid conjugates, alkylamines, fatty acids, etc. Thus, bovine gall bladder bile was mixed with an equal vol. of EtOH, centrifuged, optionally treated with activated C, concd. by evapn., and extd. with Et2O, and the aq. phase was buffered, autoclaved, and analyzed by HPLC.

MSTR 1

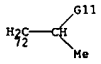
L6 ANSWER 7 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)



G1 = 51-2 52-5



G2 = CH2 / CHOH
G10 = 72



G11 = Me
MPL: claim 27

L6 ANSWER 8 OF 10 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 121:117390 MARPAT
TITLE: Cosmetic compositions containing lipids
INVENTOR(S): Parrot, David T.; Turner, Jane E.
PATENT ASSIGNEE(S): Unilever PLC, UK
SOURCE: Can. Pat. Appl., 39 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2105817	AA	19940326	CA 1993-2105817	19930909
BR 9303862	A	19940329	BR 1993-3862	19930922
AU 9347592	A1	19940331	AU 1993-47592	19930923
EP 608600	A1	19940803	EP 1993-307552	19930923
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
JP 06192658	A2	19940712	JP 1993-238412	19930924

PRIORITY APPLN. INFO.: GB 1992-20268 19920925

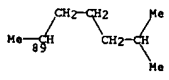
AB A smectic mesophase formed in vitro from 2 or more lipids where the lipids together form a smectic mesophase having a repeat distance (do) of >90.ANG., and the individual lipid components having a d/o of <70.ANG., and is useful for cosmetic compns. suitable for application to skin, hair or nails. The lipid components can be selected from ceramides, sterols such as cholesterol, campesterol, ergosterol or mixts. Thus, a smectic mesophase was formed from a ceramide and 5,6-dihydrocholoesterol in a mol ratio of 1:0.25. An oil-in-water emulsion was prepd. from mineral oil 4, smectic mesophase 0.1, Brij 56 4, Alfol 16RD 4, triethanolamine 0.75, 1,3-butanediol 3, xanthan gum 0.3, preservative 0.4, BHT 0.01, and water to 100% by wt. and perfume qs.

MSTR 15

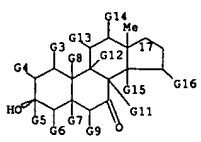
L6 ANSWER 8 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)
MPL: claim 2

G2—G1

G1 = 89



G2 = 17

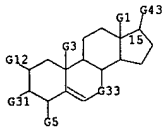


L6 ANSWER 9 OF 10 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 120:107475 MARPAT
TITLE: preparation of 4-alkenylsterols and analogs as anticholesteremics
INVENTOR(S): Archer, Robert Allen; Beavers, Lisa Selsam; Gadski, Robert Alan; Lin, Ho Shen; McClure, Don B.; McCowan, Jefferson Ray; Pawlak, Joseph Matthew; Rampersaud, Ashraff Ali; Schmidt, Robert John; et al.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 121 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 562849	A2	19930929	EP 1993-302261	19930324
EP 562849	A3	19940216		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9301117	A	19930928	NO 1993-1117	19930325
CA 2092766	AA	19930904	CA 1993-2092766	19930326
AU 9335514	A1	19930930	AU 1993-35514	19930326
HU 64082	A2	19931129	HU 1993-901	19930326
CN 1081682	A	19940209	CN 1993-105203	19930326
JP 06056670	A2	19940301	JP 1993-67968	19930326
ZA 9302178	A	19940926	ZA 1993-2178	19930326
BR 9301342	A	19931005	BR 1993-1342	19930329
PRIORITY APPLN. INFO.:			US 1992-858908	19920327
			US 1993-18985	19930303

AB Title compds. [I; R = OH, acyloxy, NH2, AcNH, etc.; R1 = (halo)alkyl; R2 = H, (halo)methyl; R3 = H, (halo)alkyl, CH2CR6:CR7R8; R4 = H, CH2Ph, (CH2)nX4; R5 = AZZ1X3; A, Z = bond, O, CHMe, CMe(OH), etc.; R6 = H, halo, (halo)alk(en)yl; R7, R8 = H, halo, (halo)methyl; R6R7 = atoms to complete a ring; X = O, H2, H and OH, H and halo, etc.; X3 = H, Ph, OPh, halo, haloalkyl, OH, etc.; X4 = H, OH, (halo) alkyl, (halo)alkoxy, etc.; Z1 = (substituted) alk(en)ylene; n = 1-16; dashed lines = optional position of optional addnl. bond] were prepd. as upregulators of LDL receptor gene expression. Thus, (+)-4-cholesten-3-one was condensed with BrCH2CH:CH2 and the product reduced to give title compd. II which reduced plasma cholesterol levels from 252 to 205 mg/dL in hypercholesteremic African green monkeys receiving 50 mg/kg/day in diet.

MSTR 1D

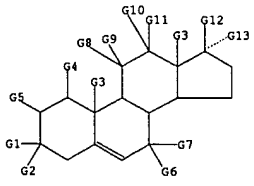


L6 ANSWER 10 OF 10 MARPAT COPYRIGHT 2002 ACS
ACCESSION NUMBER: 117:33691 MARPAT
TITLE: steroid inclusion compounds with cyclodextrin
INVENTOR(S): Agnus, Benoit; Duchene, Dominique; Wouessidjewe, Denis; Sebille, Bernard
PATENT ASSIGNEE(S): Laboratoires Besins Iscovesco, Fr.
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 477107	A1	19920325	EP 1991-402511	19910920
EP 477107	B1	19980107		
R: AT, BE, CH, DE, DK, ES, GB, GR, IT, LI, LU, NL, SE				
FR 2667070	A1	19920327	FR 1990-11687	19900921
FR 2667070	B1	19950505		
WO 9204917	A1	19920402	WO 1991-FR742	19910920
W: HU, JP, US				
AT 161732	E	19980115	AT 1991-402511	19910920
PRIORITY APPLN. INFO.:			FR 1990-11687	19900921

AB C18-27 steroids which have satd. nucleus are solubilized by forming inclusion compds. with cyclodextrins. The soly. of pregnanolone was 0.005g/L in water while with hydroxypropyl .beta.-cyclodextrin it increased to 3g/L. The inclusion compds. are for use in different pharmacetuical dosage forms.

MSTR 2A



G1 = OH
G12 = Ak (SO (1-) G14)
G6 +G7 = O
MPL: disclosure

L6 ANSWER 9 OF 10 MARPAT COPYRIGHT 2002 ACS (Continued)

G20 = alkylene (SO G46)
G31 = OH
G33 = C(O)
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: additional ring formation possible

```
=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     92.09     234.10

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -5.90      -5.90

FILE 'REGISTRY' ENTERED AT 12:26:22 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:   19 AUG 2002  HIGHEST RN 444278-83-5
DICTIONARY FILE UPDATES:  19 AUG 2002  HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 128b.str

L7      STRUCTURE UPLOADED

=> d his

     (FILE 'HOME' ENTERED AT 12:21:36 ON 20 AUG 2002)

     FILE 'REGISTRY' ENTERED AT 12:21:42 ON 20 AUG 2002
L1              STRUCTURE UPLOADED
L2            1 S L1
L3              STRUCTURE UPLOADED
L4            0 S L3
L5           26 S L3 FULL

     FILE 'MARPAT' ENTERED AT 12:24:26 ON 20 AUG 2002
L6           10 S L5 FULL

     FILE 'REGISTRY' ENTERED AT 12:26:22 ON 20 AUG 2002
L7              STRUCTURE UPLOADED

=> s l7 sub=l5 full
FULL SUBSET SEARCH INITIATED 12:26:49 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01
```

```
L8            0 SEA SUB=L5 SSS FUL L7

=> file beil
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    33.43     267.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -5.90

FILE 'BEILSTEIN' ENTERED AT 12:26:54 ON 20 AUG 2002
COPYRIGHT (c) 2002 Beilstein-Institut zur Foerderung der Chemischen Wissenschaften
licensed to Beilstein Chemiedaten & Software GmbH and MDL Information Systems GmbH

FILE RELOADED ON APRIL 8, 2002

FILE COVERS 1779 TO 2001.
*** FILE CONTAINS 8,128,462 SUBSTANCES ***

>>> For the revised summary sheet please see:
    http://info.cas.org/ONLINE/DBSS/beilsteinss.html <<<

>>> PLEASE NOTE: Reaction and substance documents are stored in
    different file segments. Use separate queries to search for
    reaction and substance data. When searching for bibliographic
    information you have the option to chose the file segment.
    (Use "/XXX.SUB" to search for a bibliographic term in
    substance documents. To restrict the search to reaction
    documents use "/XXX.RX".)
    For additional information see HELP RXS. <<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE  <<<

*********************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.               *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE  *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE         *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                       *
* FOR PRICE INFORMATION SEE HELP COST                               *
*********************************************************************

=> s l7 full
FULL SEARCH INITIATED 12:27:02 FILE 'BEILSTEIN'
FULL SCREEN SEARCH COMPLETED -    247 TO ITERATE

100.0% PROCESSED     247 ITERATIONS                          1 ANSWERS
SEARCH TIME: 00.00.05

L9            1 SEA SSS FUL L7

=> d all
```

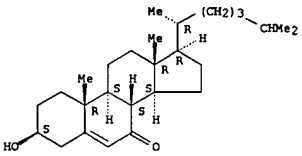
```
=> d his

     (FILE 'HOME' ENTERED AT 12:21:36 ON 20 AUG 2002)

     FILE 'REGISTRY' ENTERED AT 12:21:42 ON 20 AUG 2002
L1             STRUCTURE UPLOADED
L2           1 S L1
L3             STRUCTURE UPLOADED
L4           0 S L3
L5          26 S L3 FULL

     FILE 'MARPAT' ENTERED AT 12:24:26 ON 20 AUG 2002
L6          10 S L5 FULL

     FILE 'REGISTRY' ENTERED AT 12:26:22 ON 20 AUG 2002
L7             STRUCTURE UPLOADED
L8           0 S L7 FULL SUB=L5

     FILE 'BEILSTEIN' ENTERED AT 12:26:54 ON 20 AUG 2002
L9           1 S L7 FULL

=> d ibib ab hitstr 1-6
```

L10 ANSWER 1 OF 6 USPATFULL
ACCESSION NUMBER: 2001:131458 USPATFULL
TITLE: Process for allylic oxidation using metal hypochlorite and alkyl hydroperoxide
INVENTOR(S): Marwah, Padma, 6710 Spring Grove Ct., Middleton, WI, United States 53562
Lardy, Henry A., 1829 Thorstrand Rd., Madison, WI, United States 53705
Marwah, Ashok Kumar, 6710 Spring Grove Ct., Middleton, WI, United States 53562

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6274746	B1	20010814	
APPLICATION INFO.:	US 2000-651604		20000830	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Badio, Barbara P.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 1007
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to a process for effecting the allylic oxidation of an allylic compound having at least two allylic hydrogen atoms on the same carbon atom into corresponding .alpha.,.beta.-unsaturated carbonyl compound, using a combination of a metal hypochlorite and an alkyl hydroperoxide in a mixture of suitable conventional organic solvent(s) and/or water at a temperature of between about -5.degree. C. to +25.degree. C.
IT **566-28-9P**
(process for allylic oxidn. using metal hypochlorite and alkyl hydroperoxide)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

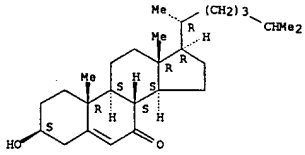


L10 ANSWER 2 OF 6 USPATFULL
ACCESSION NUMBER: 1998:147467 USPATFULL
TITLE: Reduction of hair growth
INVENTOR(S): Henry, James P., 10257 Meadow Fence Ct., Myersville, MD, United States 21773
Ahluwalia, Gurpreet S., 8632 Stableview Ct., Gaithersburg, MD, United States 20882
Shander, Douglas, 16112 Howard Landing Dr., Gaithersburg, MD, United States 20878

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5840752		19981124	
APPLICATION INFO.:	US 1996-754556		19961121	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: MacMillan, Keith D.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
LINE COUNT: 328
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mammalian hair growth is reduced by applying to the skin an inhibitor of a cholesterol synthetic pathway enzyme.
IT **566-28-9**, 7-Ketocholesterol
(skin application of inhibitors of cholesterol synthetic pathway enzymes for redn. of unwanted hair growth)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

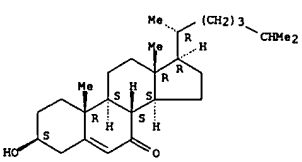


L10 ANSWER 3 OF 6 USPATFULL
ACCESSION NUMBER: 84:20038 USPATFULL
TITLE: Water-soluble cholesterol derivative
INVENTOR(S): Arakawa, Yoshio, 10-18, Ezakacho 1-chome, Suita-shi, Japan
Takanabe, Atsuyuki, 29-19, Nagao-Higashicho 2-chome, Hirakata-shi, Japan
Uemura, Yahiro, 5-18, Mitsuyacho, Hirakata-shi, Japan
Funakoshi, Satoshi, 16-5, Aoyama 1-chome, Katano-shi, Japan
Suyama, Tadakazu, 3-7, Tanabecho, Matsuigaoka 4-chome, Tsuzuki-gun, Kyoto, Japan

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4442037		19840410	
	WO 8203175		19820930	
APPLICATION INFO.:	US 1982-432938		19820928	(6)
	WO 1981-JP56		19810313	
			19820928	PCT 371 date
			19820928	PCT 102(e) date

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 314
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Complexes of albumin combined with organic dibasic acid half esters, such as those of succinic acid and phthalic acid, of 7-hydroxycholesterol are soluble in water and have excellent immunosuppressive and anti-inflammatory action.
IT **566-28-9**
(acylation of, by succinic anhydride)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



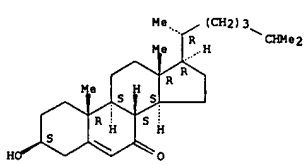
L10 ANSWER 4 OF 6 USPATFULL
ACCESSION NUMBER: 81:66945 USPATFULL
TITLE: Process for the preparation of cholesterol derivatives
INVENTOR(S): Arakawa, Yoshio, Suita, Japan
Takanabe, Atuyuki, Hirakata, Japan
Uemura, Yahiro, Hirakata, Japan
Funakoshi, Satoshi, Katano, Japan
Satoh, Daisuke, Nishinomiya, Japan
PATENT ASSIGNEE(S): The Green Cross Corporation, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4304726		19811208	
APPLICATION INFO.:	US 1980-156091		19800603	(6)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1979-76767	19790620

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 353
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB New organic dibasic acid half esters of 7-ketocholesterol and of 7-hydroxycholesterol represented by the general formula ##STR1## (wherein R.sub.1 is .dbd.O or --OH and R.sub.2 is a C.sub.1 -C.sub.5 alkylene group or a phenylene group) and physiologically acceptable salts thereof. These compounds are effective as an immunosuppressive or an anti-inflammatory agent.
IT **566-28-9**
(esterification of, by succinic anhydride)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



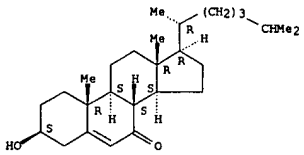
L10 ANSWER 5 OF 6 USPATFULL
ACCESSION NUMBER: 79:27040 USPATFULL
TITLE: Cholesterol derivative-based medicaments acting on bio-protective mechanisms
INVENTOR(S): Kitame, Fumio, Sendai, Japan
Saitoh, Hiroshi, Sendai, Japan
Ishida, Nakao, Sendai, Japan
PATENT ASSIGNEE(S): The Green Cross Corporation, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4157391		19790605
APPLICATION INFO.:	US 1977-804239		19770607 (5)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1977-18939	19770223

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 288
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 7-Hydroxycholesterol and 7-ketocholesterol can be used as a medicament having a pharmacodynamic action on the bio-protective mechanisms, and thus they are useful as an immunoregulatory agent or antiphlogistic agent.
IT **566-28-9P**
(prepn. of, as antiinflammatory and immunosuppressant)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

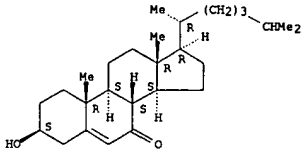


L10 ANSWER 6 OF 6 USPATFULL
ACCESSION NUMBER: 77:23980 USPATFULL
TITLE: Methods and compounds for producing specific antibodies
INVENTOR(S): Gross, Stanley J., Encino, CA, United States
PATENT ASSIGNEE(S): Biological Developments, Inc., Encino, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4022878		19770510
APPLICATION INFO.:	US 1974-528044		19741129 (5)

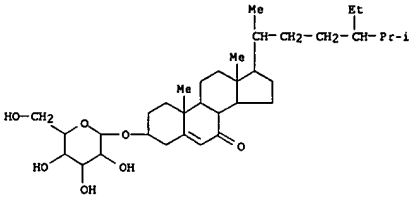
RELATED APPLN. INFO.: Division of Ser. No. US 1972-253632, filed on 15 May 1972, now abandoned which is a continuation-in-part of Ser. No. US 1970-45558, filed on 11 Jun 1970, now abandoned And Ser. No. US 1970-89929, filed on 16 Nov 1970, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Padgett, Benjamin R.
ASSISTANT EXAMINER: Nucker, Christine M.
LEGAL REPRESENTATIVE: McAulay, Fields, Fisher & Goldstein
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 774
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to a novel method of producing purified antibodies which are truly specific for native homologous hapten or antigen by administering artificial antigens as described therein to an antibody producing host followed by isolation and purification.
IT **566-28-9**
(reaction of, with carboxyphenylhydrazine, antibody prodn. in relation to)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

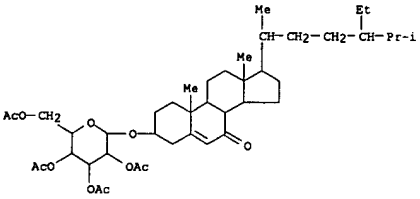


```
=> d his

     (FILE 'HOME' ENTERED AT 12:21:36 ON 20 AUG 2002)

     FILE 'REGISTRY' ENTERED AT 12:21:42 ON 20 AUG 2002
L1             STRUCTURE UPLOADED
L2           1 S L1
L3             STRUCTURE UPLOADED
L4           0 S L3
L5          26 S L3 FULL

     FILE 'MARPAT' ENTERED AT 12:24:26 ON 20 AUG 2002
L6          10 S L5 FULL

     FILE 'REGISTRY' ENTERED AT 12:26:22 ON 20 AUG 2002
L7             STRUCTURE UPLOADED
L8           0 S L7 FULL SUB=L5

     FILE 'BEILSTEIN' ENTERED AT 12:26:54 ON 20 AUG 2002
L9           1 S L7 FULL

     FILE 'USPATFULL' ENTERED AT 12:27:59 ON 20 AUG 2002
L10          6 S L5
```

L9 ANSWER 64 OF 75 USPATFULL (Continued)
IT 80666-89-3P
(prepn. of)
RN 80666-89-3 USPATFULL
CN Stigmast-5-en-7-one, 3-(.beta.-D-glucopyranosyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)



IT 80666-87-1P
(prepn., redn., and hemostatic activity of)
RN 80666-87-1 USPATFULL
CN Stigmast-5-en-7-one, 3-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)



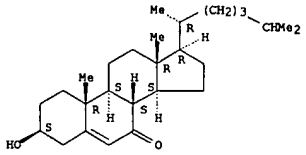
L9 ANSWER 65 OF 75 USPATFULL
ACCESSION NUMBER: 81:66945 USPATFULL
TITLE: Process for the preparation of cholesterol derivatives
INVENTOR(S): Arakawa, Yoshio, Suita, Japan
Takanabe, Atuyuki, Hirakata, Japan
Uemura, Yahiro, Hirakata, Japan
Funakoshi, Satoshi, Katano, Japan
Satoh, Daisuke, Nishinomiya, Japan
PATENT ASSIGNEE(S): The Green Cross Corporation, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4304726		19811208
APPLICATION INFO.:	US 1980-156091		19800603 (6)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1979-76767	19790620

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 353
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB New organic dibasic acid half esters of 7-ketocholesterol and of 7-hydroxycholesterol represented by the general formula ##STR1## (wherein R.sub.1 is .dbd.O or --OH and R.sub.2 is a C.sub.1 -C.sub.5 alkylene group or a phenylene group) and physiologically acceptable salts thereof. These compounds are effective as an immunosuppressive or an anti-inflammatory agent.
IT 566-28-9
(esterification of, by succinic anhydride)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

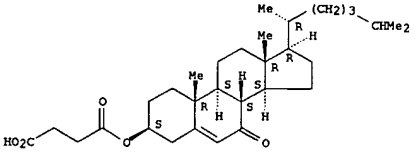
Absolute stereochemistry.



IT 78094-19-6P 78094-20-9P 78094-21-0P
78094-22-1P 78094-27-6P
(prepn. and antiinflammatory and immunosuppressive activities of)
RN 78094-19-6 USPATFULL

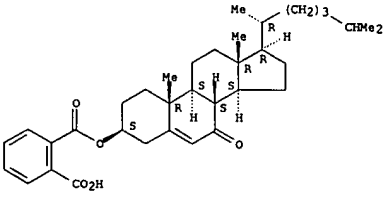
L9 ANSWER 65 OF 75 USPATFULL (Continued)
CN Cholest-5-en-7-one, 3-(3-carboxy-1-oxopropoxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 78094-20-9 USPATFULL
CN Cholest-5-en-7-one, 3-[(2-carboxybenzoyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

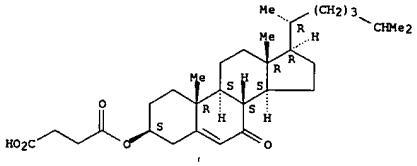
Absolute stereochemistry.



RN 78094-21-0 USPATFULL
CN Cholest-5-en-7-one, 3-(3-carboxy-1-oxopropoxy)-, sodium salt, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

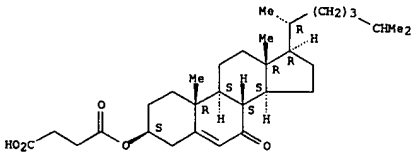
L9 ANSWER 65 OF 75 USPATFULL (Continued)



● Na

RN 78094-22-1 USPATFULL
CN Cholest-5-en-7-one, 3-(3-carboxy-1-oxopropoxy)-, ammonium salt, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● NH_3

RN 78094-27-6 USPATFULL
CN Cholest-5-en-7-one, 3-[(2-carboxybenzoyl)oxy]-, sodium salt, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 56 OF 75 USPATFULL

ACCESSION NUMBER: 94:24316 USPATFULL
TITLE: Treatment process for promoting weight loss employing a substituted .DELTA.5
INVENTOR(S): Partridge, Bruce E., Lincoln, NE, United States
Lardy, Henry A., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, Chaska, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5296481		19940322
APPLICATION INFO.:	US 1992-867288		19920410 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1990-575156, filed on 29 Aug 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Waddell, Frederick E.
ASSISTANT EXAMINER: Criares, T. J.
LEGAL REPRESENTATIVE: Faegre & Benson
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 728

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for controlling weight gain or promoting weight loss which includes the step of treating a subject with an effective weight gain controlling or weight loss promoting amount of a substituted .DELTA.5-Androstene which is biologically effective for controlling weight gain or promoting weight loss and biologically ineffective for promoting the synthesis of sex hormones. Steroids believed to provide the desired weight control/weight loss characteristics include:

.DELTA.5-Androstene-3.beta.,7.alpha.-diol-17-one

.DELTA.5-Androstene-3.beta.-ol-7,17-dione

.DELTA.5-Androstene-3.beta.,7.alpha.,17-triol

.DELTA.5-Androstene-3.beta.,17.beta.-diol-7-one

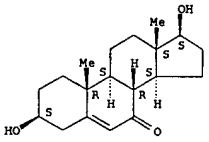
and various derivatives thereof.

IT **13209-60-4**
(glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)
RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

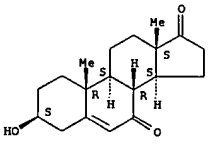
L9 ANSWER 56 OF 75 USPATFULL (Continued)

Absolute stereochemistry.



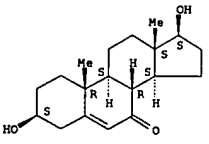
IT **566-19-8D**, esters **2226-65-5D**, esters
(wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

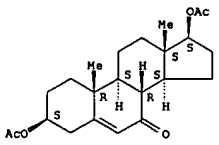


RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

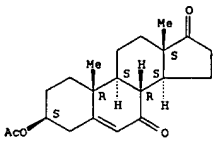


L9 ANSWER 56 OF 75 USPATFULL (Continued)



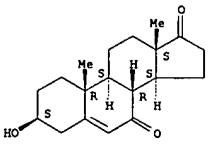
IT **1449-61-2P**
(prepn. of and glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **566-19-8P 2226-65-5P**
(prepn. of and wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

L9 ANSWER 57 OF 75 USPATFULL

ACCESSION NUMBER: 94:20165 USPATFULL
TITLE: Modulation of immune system with .DELTA.5-androstenes
INVENTOR(S): Lardy, Henry A., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, Chaska, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5292730		19940308
APPLICATION INFO.:	US 1992-922850		19920731 (7)

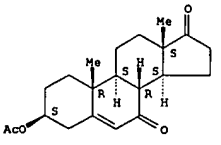
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-867288, filed on 10 Apr 1992 which is a continuation of Ser. No. US 1990-575156, filed on 29 Aug 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Waddell, Frederick E.
ASSISTANT EXAMINER: Griares, T. J.
LEGAL REPRESENTATIVE: Faegre & Benson
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 424

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Alzheimer's disease and immune deficiency disorders may be effectively treated by administering a .DELTA.5-Androstene-3.beta.-ol-17-one having a C.sub.7 substituent selected from the group consisting of oxo, hydroxy and groups convertible thereto by hydrolysis.by administering a therapeutic amount of a .DELTA.5-Androstene-3.beta.-ol-17-one having a C.sub.7 substituent selected from the group consisting of oxo, hydroxy and groups convertible thereto by hydrolysis.

IT **1449-61-2P**
(prepn. and sapon. of)
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **566-19-8P**
(prepn. of, as immunomodulator)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L9 ANSWER 52 OF 75 USPATFULL
ACCESSION NUMBER: 95:94908 USPATFULL
TITLE: Regulation of the immune system
INVENTOR(S): Loria, Roger M., 3219 Brook Rd., Richmond, VA, United States 23227

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5461042		19951024
APPLICATION INFO.:	US 1994-176234		19940103 (8)
DISCLAIMER DATE:	20110111		

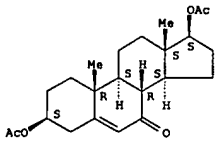
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-95431, filed on 23 Jul 1993, now abandoned And a continuation-in-part of Ser. No. US 1992-917720, filed on 24 Jul 1992, now patented, Pat. No. US 5277907 , each which is a continuation of Ser. No. US 1991-685078, filed on 15 Apr 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-437903, filed on 17 Nov 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-291969, filed on 30 Dec 1988, now patented, Pat. No. US 5077284
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Henley, III, Raymond
ASSISTANT EXAMINER: Weddington, K.
LEGAL REPRESENTATIVE: Hendricks, Glenna, Gates, Stephen
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
LINE COUNT: 977
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an improved compositions and methods for regulating the immune response, for ameliorating effects of stress, and for avoiding untoward effects of chemotherapy or exposure to irradiation by administration of androstenediol (AED) and androstenetriol (AET). The improved means of regulating immune response can be utilized in treating infectious diseases and immune diseases such as diabetes and chronic fatigue syndrome, both diseases now considered to be immune response related syndromes.

IT **13209-60-4P**, 3.beta.,17.beta.-Diacetoxyandrost-5-en-7-one (androstenediol, androstenetriol, and related compds. for immune system regulation)
RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 52 OF 75 USPATFULL (Continued)



L9 ANSWER 53 OF 75 USPATFULL
ACCESSION NUMBER: 95:52504 USPATFULL
TITLE: .DELTA.5-androstenes useful for promoting weight maintenance or weight loss and treatment process
INVENTOR(S): Lardy, Henry A., Madison, WI, United States
Reich, Ieva L., Madison, WI, United States
Wei, Yong, Washington Boro, NJ, United States
PATENT ASSIGNEE(S): Humanetics Corporation, Chaska, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5424463		19950613
APPLICATION INFO.:	US 1994-327843		19941024 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-123151, filed on 2 Sep 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-867288, filed on 10 Apr 1992, now patented, Pat. No. US 5296481 which is a continuation of Ser. No. US 1990-575156, filed on 29 Aug 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Cintins, Marianne M.
ASSISTANT EXAMINER: Criares, T. J.
LEGAL REPRESENTATIVE: Faegre & Benson
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 1348
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for promoting weight control by treating a subject with a therapeutic amount of one of the .DELTA.5-androstenes listed below to stimulate weight control without affecting appetite or inducing the synthesis of sex hormones. .DELTA.5-Androstenes providing the desired biological activities include:

.DELTA.5-Androstene-3.beta.,7.alpha.-diol-17-one

.DELTA.5-Androstene-3.beta.-ol-7,17-dione

.DELTA.5-Androstene-3.beta.,7.alpha.,17.beta.-triol

.DELTA.5-Androstene-3.beta.,17.beta.-diol-7-one

.DELTA.5-Androstene-3.beta.-acetoxy-7,16,17-trione

.DELTA.5-Androstene-3.beta.,16.alpha.-dihydroxy-7,17-dione

.DELTA.5-Androstene-3.alpha.-propionoxy-16.beta.-acetoxy-7,17-dione

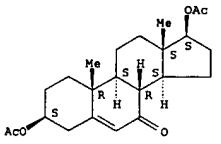
.DELTA.5-Androstene-3.beta.,7.alpha.,17.beta.-triol-16-one

.DELTA.5-Androstene-3.beta.,17.beta.-diol-7,16-dione

.DELTA.5-Androstene-3.beta.,16.alpha.,17.beta.-triol-7-one.

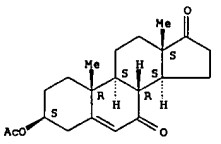
IT **13209-60-4**
(glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)
RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

L9 ANSWER 53 OF 75 USPATFULL (Continued)
Absolute stereochemistry.



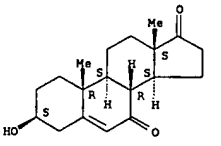
IT **1449-61-2P**
(prepn. of and glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **566-19-8P 2226-65-5P**
(prepn. of and wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 48 OF 75 USPATFULL
ACCESSION NUMBER: 96:43382 USPATFULL
TITLE: Vaccine compositions and method for induction of mucosal immune response via systemic vaccination
INVENTOR(S): Daynes, Raymond A., Park City, UT, United States
Araneo, Barbara A., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): University of Utah Research Foundation, Salt Lake City, UT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5518725		19960521
APPLICATION INFO.:	US 1993-123844		19930909 (8)

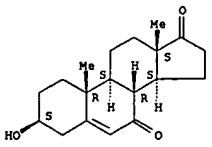
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-13972, filed on 4 Feb 1993, now abandoned And a continuation-in-part of Ser. No. US 1991-779499, filed on 18 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-412270, filed on 25 Sep 1989, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Sidberry, Hazel F.
ASSISTANT EXAMINER: Krsek-Staples, Julie
LEGAL REPRESENTATIVE: Venable, Baetjer, Howard & Civiletti
NUMBER OF CLAIMS: 63
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 56 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 1760
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a vaccine which comprises an antigen and a lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include 1,25-dihydroxy Vitamin D.sub.3, biologically active Vitamin D.sub.3 derivatives which are capable of activating the intracellular Vitamin D.sub.3 receptor, all trans-retinoic acid, retinoic acid derivatives, retinol, retinol derivatives and glucocorticoid. The vaccine composition may further comprise an immune response augmenting agent which enhances T cell lymphokine production. Suitable immune response augmenting agents include dehydroepiandrosterone (DHEA) and DHEA-derivatives. Examples of DHEA derivatives include DHEA-sulfate (DHEA-S), 16-.alpha.-bromo-DHEA, 7-oxo-DHEA, 16-.alpha.-Br-DHEA-S and 7-oxo-DHEA-S. The invention also relates to a method for inducing an antigen-specific mucosal immune response in a vertebrate animal which comprises administering a vaccine which comprises an antigen and a lymphoid organ modifying agent with or without an immune response augmenting agent to a site which drains into a peripheral lymphoid compartment.

IT **566-19-8**, 7-Oxodehydroepiandrosterone **4121-96-4**, 7-Oxo-5,6-dehydroepiandrosterone sulfate
(vaccine compns. and method for induction of mucosal immune response via systemic vaccination)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

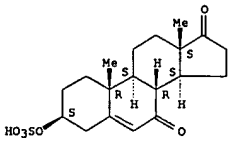
Absolute stereochemistry. Rotation (-).

L9 ANSWER 48 OF 75 USPATFULL (Continued)



RN 4121-96-4 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 49 OF 75 USPATFULL
ACCESSION NUMBER: 96:29552 USPATFULL
TITLE: .DELTA.5-androstenes useful for promoting weight maintenance or weight loss and treatment process
INVENTOR(S): Lardy, Henry A., Madison, WI, United States
Reich, Ieva L., Madison, WI, United States
Wei, Yong, Washington Boro, NJ, United States
PATENT ASSIGNEE(S): Humanetics Corporation, St. Louis Park, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5506223		19960409
APPLICATION INFO.:	US 1994-327646		19941024 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1993-123151, filed on 2 Sep 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-867288, filed on 10 Apr 1992, now patented, Pat. No. US 5296481 which is a continuation of Ser. No. US 1990-575156, filed on 29 Aug 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Faegre & Benson
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 1312
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for promoting weight control by treating a subject with a therapeutic amount of one of the .DELTA.5-androstenes listed below to stimulate weight control without affecting appetite or inducing the synthesis of sex hormones.

.DELTA.5-Androstenes providing the desired biological activities include:

.DELTA.5-Androstene-3.beta.,7.alpha.-diol-17-one (1)

.DELTA.5-Androstene-3.beta.-ol-7,17-dione (2)

.DELTA.5-Androstene-3.beta.,7.alpha.,17.beta.-triol (3)

.DELTA.5-Androstene-3.beta.,17.beta.-diol-7-one (4)

.DELTA.5-Androstene-3.beta.-acetoxy-7,16,17-trione (5)

.DELTA.5-Androstene-3.beta.,16.alpha.-dihydroxy-7,17-dione (6)

.DELTA.5-Androstene-3.beta.-propionoxy-16.beta.-acetoxy-7,17-dione (7)

.DELTA.5-Androstene-3.beta.,7.alpha.,17.beta.-triol-16-one (8)

.DELTA.5-Androstene-3.beta.,17.beta.-diol-7,16-dione (9)

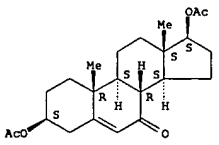
.DELTA.5-Androstene-3.beta.,16.alpha.,17.beta.-triol-7-one (10)

and derivatives thereof wherein one or more of the hydroxyl or keto substituents is a group convertible thereto by hydrolysis.

IT **13209-60-4**
(glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)

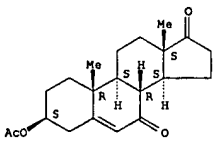
L9 ANSWER 49 OF 75 USPATFULL (Continued)
RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



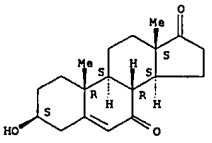
IT **1449-61-2P**
(prepn. of and glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **566-19-8P 2226-65-5P**
(prepn. of and wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX

L7 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:167790 CAPLUS
DOCUMENT NUMBER: 134:217169
TITLE: Oxysterols for modulating HDL cholesterol and triglyceride levels by modulating LXR-mediated transcription
INVENTOR(S): Hayden, Michael R.; Brooks-Wilson, Angela R.; Pimstone, Simon N.; Clee, Susanne M.
PATENT ASSIGNEE(S): University of British Columbia, Can.; Xenon Genetics, Inc.
SOURCE: PCT Int. Appl., 316 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015676	A2	20010308	WO 2000-IB1492	20000901
WO 2001015676	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-151977P P 19990901
US 2000-526193 A 20000315
US 2000-213958P P 20000623

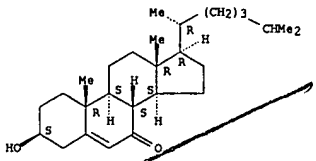
AB The invention features methods for treating patients having low HDL, a higher than normal triglyceride level, or a cardiovascular disease by administering compds. that modulate ABC1 expression or activity. Compds. of the invention include oxysterols that modulate LXR-mediated transcription.

IT **566-28-9**, 7-Oxocholesterol **220066-66-0**, 7-Oxo-24(S),25-epoxycholesterol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process)
USES (Uses)
(oxysterols for modulating HDL cholesterol and triglyceride levels by modulating LXR-mediated transcription)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

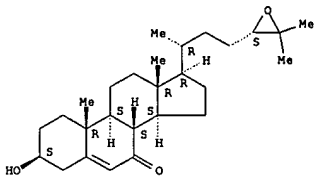
Absolute stereochemistry.

L7 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 220066-66-0 CAPLUS
CN Cholest-5-en-7-one, 24,25-epoxy-3-hydroxy-, (3.beta.,24S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



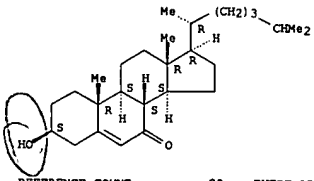
L7 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:87328 CAPLUS
DOCUMENT NUMBER: 135:17931
TITLE: Comparative analysis of plasma and erythrocyte 7-ketocholesterol as a marker for oxidative stress in patients with diabetes mellitus
AUTHOR(S): Abo, Katsumi; Mio, Takaya; Sumino, Kimiaki
CORPORATE SOURCE: Department of Public Health, Kobe University School of Medicine, Kobe, 650-0017, Japan
SOURCE: Clinical Biochemistry (2000), 33(7), 541-547
CODEN: CLBIAS; ISSN: 0009-9120
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objectives: To reveal increased lipid peroxidn. in diabetics by quantification of cholesterol oxidn. products (COPs) not only in plasma, but also in erythrocytes. Design and methods: We quantified 7-ketocholesterol (7-kCho) by gas chromatog.-mass spectrometry as a surrogate measure for COPs. These assays were performed on both plasma and erythrocytes in 20 control subjects and 20 treated patients with relatively poorly controlled Type 2 diabetes. Results: Both plasma and erythrocyte 7-kCho levels in diabetics were significantly higher than those in control subjects. Although neither plasma nor erythrocyte 7-kCho levels were assocd. with markers for glucose tolerance in diabetics, a neg. correlation of serum HDL-cholesterol levels with erythrocyte, but not plasma, 7-kCho levels was found. Conclusion: Increased oxidative stress in diabetics affects oxidn. of cholesterol. Assays of COPs not only in plasma, but also in erythrocytes, may yield complementary information in lipid peroxidn.

IT **566-28-9**, 7-Ketocholesterol
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence)
USES (Uses)
(comparative anal. of plasma and erythrocyte 7-ketocholesterol as a marker for oxidative stress in human patients with diabetes mellitus)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:830402 CAPLUS
DOCUMENT NUMBER: 134:1043
TITLE: Memory enhancement by the administration of .delta.5-androstene-3.beta.-ol-7,17-dione and 3.beta. esters thereof
INVENTOR(S): Lardy, Henry A.; Shi, Jennifer Y.
PATENT ASSIGNEE(S): Humanetics Corporation, USA
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6153606	A	20001128	US 1998-174235	19981016
EP 1123100	A1	20010816	EP 1999-954931	19991013

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

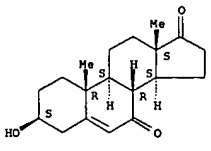
PRIORITY APPLN. INFO.: US 1998-174235 A 19981016
WO 1999-US24076 W 19991013

AB The memory of a healthy mammal and the memory of a mammal with age impaired memory can be improved by administering an effective amt. of .DELTA.5-Androstene-3.beta.-ol-7,17-dione and 3.beta. esters thereof.

IT **566-19-8** **566-19-8D**, 3.beta.-esters
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(memory enhancement by administration of .DELTA.5-androstene-3.beta.-ol-7,17-dione and 3.beta. esters thereof)

RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

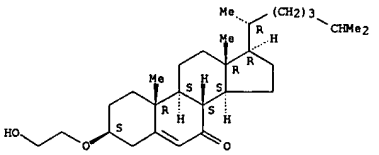


RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L7 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:752281 CAPLUS
DOCUMENT NUMBER: 126:84406
TITLE: Steryl cellosolves regulate cholesterol metabolism in isolated rabbit hepatocytes
AUTHOR(S): Malyugin, A. V.; Shteinshneider, A. Yu.; Kosykh, V. A.; Alquier, Ch.; Lafont, H.; Misharin, A. Yu.
CORPORATE SOURCE: Inst. Eksper.Kardiol., RAMN, Moscow, 121552, Russia
SOURCE: Bioorganicheskaya Khimiya (1996), 22(8), 606-610
CODEN: BIKHD7; ISSN: 0132-3423
PUBLISHER: MAIK Nauka
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Synthesis of 3.beta.-(2-hydroxyethoxy)cholest-5-ene, 3.beta.-(2-hydroxyethoxy)cholest-5-en-7-one, 3.beta.-(2-hydroxyethoxy)-7.beta.-hydroxycholest-5-ene, 3.beta.-(2-hydroxyethoxy)-5.alpha.,6.beta.-dihydroxycholestane is described. These substances inhibited cholesterol biosynthesis in rabbit hepatocyte cell culture with ID50 from 5.5(.+-.0.7) x 10-8 to 1.3(.+-.0.2) x 10-5 M and also cellular protein biosynthesis.
IT **155252-30-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of and hepatocyte cholesterol metab. regulation by hydroxyethoxy cholestanes and cholestenes)
RN 155252-30-5 CAPLUS
CN Cholest-5-en-7-one, 3-(2-hydroxyethoxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



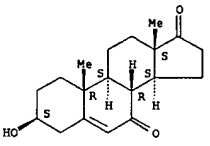
L7 ANSWER 30 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:637506 CAPLUS
DOCUMENT NUMBER: 126:6438
TITLE: Vaccine compositions and method for enhancing an immune response
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 34 pp., Cont-in-part of U. S. Ser. No. 13,972, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5562910	A	19961008	US 1993-123843	19930909
US 5827841	A	19981027	US 1994-295068	19940920
US 5753237	A	19980519	US 1994-309704	19940921
US 5919465	A	19990706	US 1994-309717	19940921
US 5837269	A	19981117	US 1995-487173	19950607

PRIORITY APPLN. INFO.: US 1989-412270 19890925
US 1991-779499 19911018
US 1993-13972 19930204
US 1993-18471 19930216
US 1993-123843 19930909
US 1994-219418 19940329
OTHER SOURCE(S): MARPAT 126:6438
AB The invention relates to a vaccine which comprises an antigen and an immune response augmenting agent. The immune response augmenting agent is capable of enhancing T cell lymphokine prodn. Suitable immune response augmenting agents include, but are not limited to, dehydroepiandrosterone (DHEA) and DHEA-derivs. Examples of DHEA derivs. include DHEA-sulfate (DHEA-S), 16.alpha.-bromo-DHEA, 7-oxo-DHEA, 16.alpha.-bromo-DHEA-S and 7-oxo-DHEA-S. The invention also relates to a method for enhancing a vaccine-induced humoral immune response which comprises administering a vaccine which comprises an antigen and an immunomodulator. The immunomodulator may be an immune response augmenting agent, a lymphoid organ modifying agent or a mixt. of the immune response augmenting agent and lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include, but are not limited to, 1,25-dihydroxy Vitamin D3, biol. active Vitamin D3 derivs. which are capable of activating the intracellular Vitamin D3 receptor, all trans-retinoic acid, retinoic acid derivs., retinol, retinol derivs. and glucocorticoid. Alternatively, the method for enhancing a vaccine-induced humoral immune response comprises sep. administering the immunomodulator and a vaccine contg. an antigen.
IT **566-19-8 4121-96-4**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(vaccine comprises antigen and immunomodulator or lymphoid organ modifying agent)
RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

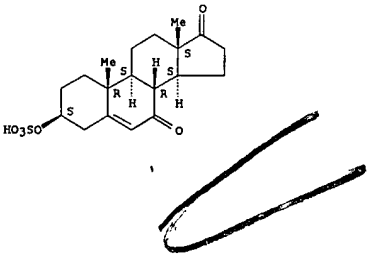
Absolute stereochemistry. Rotation (-).

L7 ANSWER 30 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:366050 CAPLUS
DOCUMENT NUMBER: 125:41730
TITLE: Vaccine compositions and method for induction of mucosal immune response via systemic vaccination
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 13,972, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5518725	A	19960521	US 1993-123844	19930909
CA 2153794	AA	19940818	CA 1994-2153794	19940203
WO 9417823	A1	19940818	WO 1994-US1220	19940203
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9462348	A1	19940829	AU 1994-62348	19940203
AU 679215	B2	19970626		
EP 686042	A1	19951213	EP 1994-909530	19940203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 72404	A2	19960429	HU 1995-2105	19940203
JP 08508718	T2	19960917	JP 1994-518202	19940203
US 5827841	A	19981027	US 1994-295068	19940920
US 5753237	A	19980519	US 1994-309704	19940921
US 5919465	A	19990706	US 1994-309717	19940921
US 5824313	A	19981020	US 1995-480567	19950607
FI 9503608	A	19950919	FI 1995-3608	19950728
NO 9503049	A	19951003	NO 1995-3049	19950803

PRIORITY APPLN. INFO.: US 1989-412270 19890925
US 1991-779499 19911018
US 1993-13972 19930204
US 1993-18471 19930216
US 1993-123844 19930909
WO 1994-US1220 19940203
US 1994-219418 19940329
AB The invention relates to a vaccine which comprises an antigen and a lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include 1,25-dihydroxy Vitamin D3, biol. active Vitamin D3 derivs. which are capable of activating the intracellular Vitamin D3 receptor, all trans-retinoic acid, retinoic acid derivs., retinol, retinol derivs. and glucocorticoid. The vaccine compn. may further comprise an immune response augmenting agent which enhances T cell lymphokine prodn. Suitable immune response augmenting agents include dehydroepiandrosterone (DHEA) and DHEA-derivs. Examples of DHEA derivs. include DHEA-sulfate (DHEA-S), 16-.alpha.-bromo-DHEA, 7-oxo-DHEA, 16-.alpha.-Br-DHEA-S and 7-oxo-DHEA-S. The invention also relates to a method for inducing an antigen-specific mucosal immune response in a vertebrate animal which comprises administering a vaccine which comprises an antigen and a lymphoid organ modifying agent with or without an immune response augmenting agent to a site which drains into a peripheral lymphoid compartment.
IT **566-19-8, 7-Oxodehydroepiandrosterone 4121-96-4,**
7-Oxo-5,6-dehydroepiandrosterone sulfate

L7 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:344832 CAPLUS
DOCUMENT NUMBER: 131:1145
TITLE: Use of .DELTA.5-androstene-3.beta.-ol-7,17-dione in the treatment of arthritis
INVENTOR(S): Weeks, Charles E.
PATENT ASSIGNEE(S): Humanetics Corporation, USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925192	A1	19990527	WO 1998-US24458	19981117
W: AU, CA, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2311471	AA	19990527	CA 1998-2311471	19981117
AU 9914142	A1	19990607	AU 1999-14142	19981117
EP 1032266	A1	20000906	EP 1998-958020	19981117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-66197P P 19971119
WO 1998-US24458 W 19981117

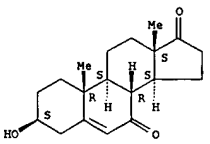
AB Arthritis can be treated by administering therapeutic amts. of .DELTA.5-androstene-3.beta.-ol-7,17-dione and metabolizable precursors thereof, such as .DELTA.5-androstene-3.beta.-acetoxy-7,17-dione, which are readily metabolized in vivo to .DELTA.5-androstene-3.beta.-ol-7,17-dione but are not appreciably metabolizable in vivo to androgens, estrogens or dehydroepiandrosterone. Such treatment can be prophylactic, ameliorative or curative in nature.

IT **566-19-8D**, precursors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(.DELTA.5-androstene-3.beta.-ol-7,17-dione and metabolizable precursors in the treatment of arthritis)

RN 566-19-8 CAPLUS

CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



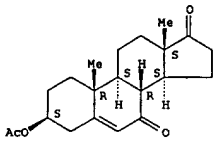
L7 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)

IT **1449-61-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(.DELTA.5-androstene-3.beta.-ol-7,17-dione and metabolizable precursors in the treatment of arthritis)

RN 1449-61-2 CAPLUS

CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

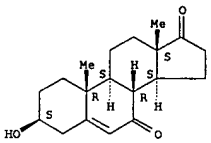


IT **566-19-8DP**, precursors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(.DELTA.5-androstene-3.beta.-ol-7,17-dione and metabolizable precursors in the treatment of arthritis)

RN 566-19-8 CAPLUS

CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:749358 CAPLUS
DOCUMENT NUMBER: 130:17243
TITLE: Vaccine compositions and method for enhancing an immune response
INVENTOR(S): Daynes, Raymond A.; Araneo, Barbara A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: U.S., 38 pp., Cont.-in-part o f U. S. 5,562,910.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5837269	A	19981117	US 1995-487173	19950607
US 5562910	A	19961008	US 1993-123843	19930909
US 5827841	A	19981027	US 1994-295068	19940920
US 5753237	A	19980519	US 1994-309704	19940921
US 5919465	A	19990706	US 1994-309717	19940921

PRIORITY APPLN. INFO.: US 1989-412270 19890925
US 1991-779499 19911018
US 1993-13972 19930204
US 1993-123843 19930909
US 1993-18471 19930216
US 1994-219418 19940329

OTHER SOURCE(S): MARPAT 130:17243

AB The invention relates to a vaccine which comprises an antigen and an immune response-augmenting agent. The immune response-augmenting agent is capable of enhancing T cell lymphokine prodn. Suitable immune response augmenting agents include, but are not limited to, DHEA, DHEA-derivs. and DHEA congeners. The invention also relates to a method for enhancing a vaccine-induced humoral immune response which comprises administering a vaccine which comprises an antigen and an immunomodulator. The immunomodulator may be an immune response augmenting agent, a lymphoid organ modifying agent or a mixt. of the immune response augmenting agent and lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include, but are not limited to, 1,25-dihydroxy Vitamin D3, 25-hydroxy Vitamin D3, biol. active 1,25-dihydroxy Vitamin D3, derivs. which are capable of activating the intra-cellular Vitamin D3 receptor, all trans-retinoic acid, retinoic acid derivs., retinol, retinol derivs. and glucocorticoid. Alternatively, the method for enhancing a vaccine-induced humoral immune response comprises sep. administering the immunomodulator and a vaccine contg. an antigen.

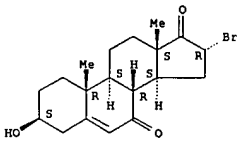
IT **216062-79-2 216062-88-3 216062-89-4 216062-99-6 216063-03-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(vaccine compns. and method for enhancing an immune response)

RN 216062-79-2 CAPLUS

CN Androst-5-ene-7,17-dione, 16-bromo-3-hydroxy-, (3.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

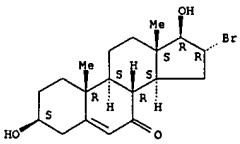
L7 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 216062-88-3 CAPLUS

CN Androst-5-en-7-one, 16-bromo-3,17-dihydroxy-, (3.beta.,16.alpha.,17.beta.)- (9CI) (CA INDEX NAME)

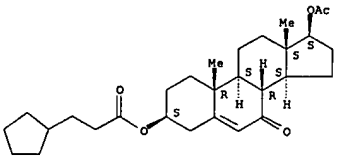
Absolute stereochemistry.



RN 216062-89-4 CAPLUS

CN Androst-5-en-7-one, 17-(acetyloxy)-3-(3-cyclopentyl-1-oxopropoxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

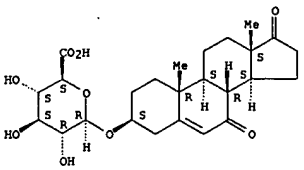


RN 216062-99-6 CAPLUS

CN .beta.-D-Glucopyranosiduronic acid, (3.beta.)-7,17-dioxoandrost-5-en-3-yl (9CI) (CA INDEX NAME)

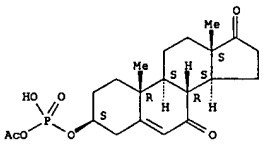
Absolute stereochemistry.

L7 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 216063-03-5 CAPLUS
CN Androst-5-ene-7,17-dione, 3-[[(acetyloxy)hydroxyphosphinyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:509107 CAPLUS
DOCUMENT NUMBER: 129:131694
TITLE: Use of .DELTA.5-androstenes in the treatment of HIV wasting syndrome
INVENTOR(S): Pauza, C. David; Lardy, Henry A.
PATENT ASSIGNEE(S): Humanetics Corp., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831371	A1	19980723	WO 1998-US766	19980115
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5885977	A	19990323	US 1997-784856	19970115
AU 9859190	A1	19980807	AU 1998-59190	19980115
EP 1014992	A1	20000705	EP 1998-902561	19980115
R: DE, GB				

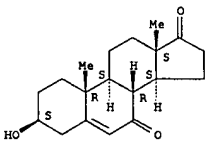
PRIORITY APPLN. INFO.: US 1997-784856 A 19970115
WO 1998-US766 W 19980115

AB HIV-related wt. loss, HIV-related cachexia and HIV-related wasting syndrome can be treated by administering therapeutic amts. of the steroid .DELTA.5-androstene-3.beta.-ol-7,17 dione and metabolizable precursors thereof, such as .DELTA.5-androstene-3.beta.-acetoxy-7,17 dione, which are readily metabolized in vivo to .DELTA.5-androstene-3.beta.-ol-7,17 dione. Such treatment can be prophylactic, modulatory, ameliorative or curative in nature.

IT **566-19-8DP**, precursors **1449-61-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use of .DELTA.5-androstenes in treatment of HIV wasting syndrome)

RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

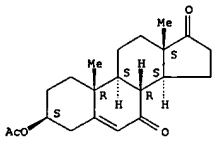
Absolute stereochemistry. Rotation (-).



RN 1449-61-2 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX

L7 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)
NAME)

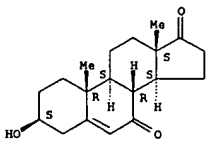
Absolute stereochemistry.



IT **566-19-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. and use of .DELTA.5-androstenes in treatment of HIV wasting syndrome)

RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



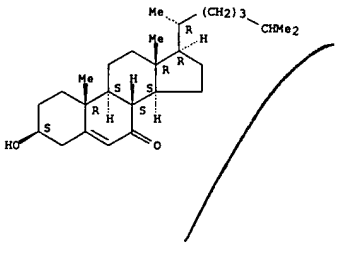
L7 ANSWER 25 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:417233 CAPLUS
DOCUMENT NUMBER: 129:156591
TITLE: Inhibition of p42/p44 mitogen-activated protein kinase by oxysterols in rat astrocyte primary cultures and C6 glioma cell lines
AUTHOR(S): Adamczyk, Monika; Scherrer, Elisabeth; Kupferberg, Alexandre; Malviya, Anant N.; Mersel, Marcel
CORPORATE SOURCE: Centre of Neurochemistry, CNRS, Strasbourg, Fr.
SOURCE: Journal of Neuroscience Research (1998), 53(1), 38-50
CODEN: JNRESDK; ISSN: 0360-4012
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We previously demonstrated that oxysterols inhibit the growth of exptl. glioblastoma induced in the rat brain cortex. Mechanism of action of these compds. remains obscure. In this study, we investigated the effect of 7.beta.-hydroxycholesterol (7.beta.-OHCH) and 7-ketocholesterol (7k-CH) on the growth and MAP kinase activity in three in vitro biol. models: rat astrocyte primary cultures, primary cultures treated by dibutyryl-cAMP (reactive cells), and the C6 glioma cell line. The oxysterols are not lethal to primary astrocytes, even if MAP kinase activity is decreased, particularly when cells were treated with 7k-CH. Both oxysterols are toxic to reactive astrocytes, and as compared with untreated primary cultures, they amplified the MAP kinase activity decrease. However, the mechanism of action of oxysterols on reactive astrocytes seems not to be linked to the MAP kinase pathway. In highly proliferating C6 cell lines, only 7.beta.-OHCH has an antiproliferative effect and is cytotoxic. The inhibition of MAP kinase activity is a function of 7.beta.-OHCH concn. PD098059, a MAP kinase pathway inhibitor, has only a time-limited antiproliferative effect on C6 cell growth. We conclude that in C6 cells, the MAP kinase activity decrease is correlated with the toxic effect of 7.beta.-OHCH and occurs at first stages of 7.beta.-OHCH action.

IT **566-28-9**, 7-Ketocholesterol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibition of p42/p44 mitogen-activated protein kinase by oxysterols in rat astrocyte primary cultures and C6 glioma cell lines)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



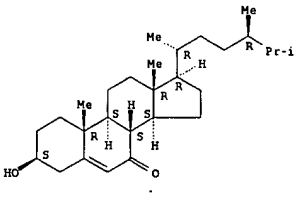
L7 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:493647 CAPLUS
DOCUMENT NUMBER: 132:113143
TITLE: Phytosterol oxides in some samples of pure phytosterols mixture and in a few tablet supplement preparations in Finland
AUTHOR(S): Dutta, Paresh C.
CORPORATE SOURCE: Department of Food Science, Swedish University of Agricultural Sciences, Uppsala, 750 07, Swed.
SOURCE: Special Publication - Royal Society of Chemistry (1999), 240(Natural Antioxidants and Anticarcinogens in Nutrition, Health and Disease), 316-319
CODEN: SROCDO; ISSN: 0260-6291
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Detns. were made of polar oxidn. products of phytosterols in raw materials (wood sterols) and in a no. of supplement tablet prepns. contg. photosterols com. available in Finland. In addn., a sample of pure phytosterol mixt. was subjected to oxidn. by treatment at high temp. was analyzed and compared with the unheated raw materials. The content of total polar oxidized sterols in the wood sterols and recrystd. sterols were 75 mg/100g and 44 mg/100g, resp., whereas the heat-treated sterols had 1380 mg/100g. The table prepns. Anti K-steroli, Tri Tolosen Kasvisteroli, and Kolestop (trade names fro com. phytosterol supplement products) had the total polar oxidn. products of 14 mg/100 g, 26 mg/100 g, and 30 mg/100 g tablets, resp. Only 6 of the polar oxidn. products were identified by GC-MS by comparing the mass spectra with those of authentic samples. Among the polar oxidized phytosterols identified, the highest amts. obsd. were epimers of epoxycampesterol and sitosterol, and 7-ketocampesterol and sitosterol. In the tablet prepns, amts. of epoxysterols ranged 5-14 mg/100 g, and 7-ketosterols ranged 3-5 mg/100g.

IT **55396-22-0**, 7-Ketocampesterol
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(phytosterol oxides in pure phytosterol mixts. and in tablet supplement prepns. in Finland)

RN 55396-22-0 CAPLUS
CN Ergost-5-en-7-one, 3-hydroxy-, (3.beta.,24R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:350591 CAPLUS
DOCUMENT NUMBER: 131:1146
TITLE: Use of .DELTA.5-androstene-3.beta.-ol-7,17-dione in the treatment of lupus erythematosus
INVENTOR(S): Lardy, Henry A.; Weeks, Charles E.
PATENT ASSIGNEE(S): Humanetics Corporation, USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925333	A1	19990527	WO 1998-US23386	19981103
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2310632	AA	19990527	CA 1998-2310632	19981103
AU 9913017	A1	19990607	AU 1999-13017	19981103
AU 738136	B2	20010906		
EP 1032380	A1	20000906	EP 1998-956509	19981103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6372732	B1	20020416	US 2000-554952	20001204

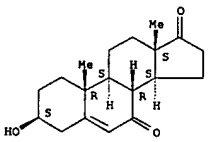
PRIORITY APPLN. INFO.: US 1997-66198P P 19971119
WO 1998-US23386 W 19981103

AB Lupus erythematosus can be treated by administering therapeutic amts. of .DELTA.5-androstene-3.beta.-ol-7,17-dione and metabolizable precursors thereof, such as .DELTA.5-androstene-3.beta.-acetoxy-7,17-dione, which are readily metabolized in vivo to .DELTA.5-androstene-3.beta.-ol-7,17-dione but are not appreciably metabolizable in vivo to androgens, estrogens or dehydroepiandrosterone. Such treatment can be prophylactic, ameliorative or curative in nature.

IT **566-19-8D**, precursors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(.DELTA.5-androstene-3.beta.-ol-7,17-dione and metabolizable precursors in the treatment of lupus erythematosus)

RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

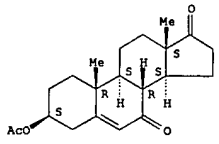


IT **1449-61-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

L7 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)
study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(.DELTA.5-androstene-3.beta.-ol-7,17-dione and metabolizable precursors in the treatment of lupus erythematosus)

RN 1449-61-2 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

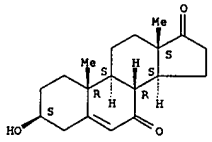
Absolute stereochemistry.



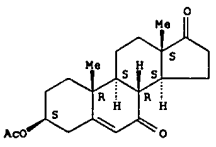
IT **566-19-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(.DELTA.5-androstene-3.beta.-ol-7,17-dione and metabolizable precursors in the treatment of lupus erythematosus)

RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:412729 CAPLUS
DOCUMENT NUMBER: 133:133759
TITLE: Cholesterol movement in Niemann-Pick type C cells and in cells treated with amphiphiles
AUTHOR(S): Lange, Yvonne; Ye, Jin; Rigney, Mike; Steck, Theodore
CORPORATE SOURCE: Department of Pathology, Rush-Presbyterian-St. Luke's Medical Center, University of Chicago, Chicago, IL, 60637, USA
SOURCE: Journal of Biological Chemistry (2000), 275(23), 17468-17475
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

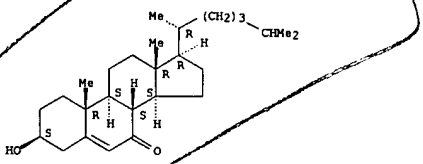
AB Cholesterol accumulates to massive levels in cells from Niemann-Pick type C (NP-C) patients and in cells treated with class 2 amphiphiles that mimic NP-C disease. This behavior has been attributed to the failure of cholesterol released from ingested low d. lipoproteins to exit the lysosomes. However, the authors now show that the rate of movement of cholesterol from lysosomes to plasma membranes in NP-C cells is at least as great as normal, as was also found previously for amphiphile-treated cells. Furthermore, the lysosomes in these cells filled with plasma membrane cholesterol in the absence of lipoproteins. In addn., the authors showed that the size of the endoplasmic reticulum cholesterol pool and the set point of the homeostatic sensor of cell cholesterol were approx. normal in NP-C cells. The plasma membrane cholesterol pools in both NP-C and amphiphile-treated cells were also normal. Furthermore, the build up of cholesterol in NP-C lysosomes was not a physiol. response to cholesterol overload. Rather, it appeared that the accumulation in NP-C lysosomes results from an imbalance in the brisk flow of cholesterol among membrane compartments. In related expts., the authors found that NP-C cells did not respond to class 2 amphiphiles (e.g. trifluoperazine, imipramine, and U18666A); these agents may therefore act directly on the NPC1 protein or on its pathway. Finally, the authors showed that the lysosomal cholesterol pool in NP-C cells was substantially and preferentially reduced by incubating cells with the oxysterols, 25-hydroxycholesterol and 7-ketocholesterol; these findings suggest a new pharmacol. approach to the treatment of NP-C disease.

IT **566-28-9**, 7-Ketocholesterol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lysosomal cholesterol pool in human Niemann-Pick type C cells was substantially and preferentially reduced by incubating cells with oxysterols, 25-hydroxycholesterol and 7-ketocholesterol)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2002 ACS

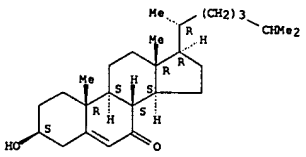
ACCESSION NUMBER: 2000:243980 CAPLUS
DOCUMENT NUMBER: 133:15832
TITLE: Plasma oxysterols and tocopherol in patients with diabetes mellitus and hyperlipidemia
AUTHOR(S): Murakami, Hiroshi; Tamasawa, Naoki; Matsui, Jun; Yasujima, Minoru; Suda, Toshihiro
CORPORATE SOURCE: Third Department of Internal Medicine, Hirosaki University School of Medicine, Hirosaki, 036-8562, Japan
SOURCE: Lipids (2000), 35(3), 333-338
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The plasma levels of free oxysterols (7-ketocholesterol; 7.alpha.-hydroxy-,7.beta.-hydroxy-, 25-hydroxy-, and 27-hydroxycholesterol; and 5.alpha.,6.alpha.-epoxycholestanol) in patients with diabetes mellitus and hypercholesterolemia were detd. using gas chromatog.-mass spectrometry with selective ion monitoring. We studied 39 patients with diabetes mellitus, 20 nondiabetic patients with hypercholesterolemia, and 37 normal controls. Plasma cholesterol levels in diabetic and hypercholesterolemic patients showed no statistical difference. Plasma 7-ketocholesterol was significantly higher in patients with diabetes (31.6 .+-. 2.8 ng/mL) or hypercholesterolemia (52.3 .+-. 5.9) than in the control group (22.4 .+-. 1.2). The increased plasma cholesterol can be regarded as an oxidn. substrate for the oxidant stress and the higher abs. levels of oxysterols in hypercholesterolemic plasma compared with the control plasma. This difference disappeared when 7-ketocholesterol was expressed in proportion to total cholesterol. The oxidizability of plasma cholesterol was evaluated by comparing the increased ratio of 7-ketocholesterol after CuSO4 oxidn. to the ratio before. We demonstrated that the patients with diabetes showed increased oxidizability (77.5%) compared with the control (36.6%) or hyperlipemic group (45.3%), which is likely due to the lower amts. of .alpha.-tocopherol in the diabetics. Measurement of oxysterols may serve as a marker for in vivo oxidized lipoproteins in diabetes and hyperlipemia.

IT **566-28-9**, 7-Ketocholesterol
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(oxysterols and tocopherol in human plasma in diabetes mellitus and hyperlipidemia as marker of oxidn.)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



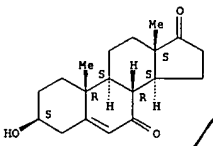
=> d ibib ab hitstr 1-41

L7 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:465783 CAPLUS
DOCUMENT NUMBER: 137:37386
TITLE: Use of 7-hydroxy DHEA and/or 7-keto DHEA for treating disorders related to excessive 5.alpha.-reductase activity
INVENTOR(S): Picard-Lesboueyries, Elisabeth
PATENT ASSIGNEE(S): L'Oreal, Fr.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047651	A1	20020620	WO 2001-FR3730	20011126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2818132	A1	20020621	FR 2000-16433	20001215

PRIORITY APPLN. INFO.: FR 2000-16433 A 20001215
AB The invention concerns the use of a DHEA deriv. selected among 7-hydroxy DHEA and/or 7-keto DHEA in or for prepg. a compn. for preventing or treating disorders related to excessive 5.alpha.-reductase activity such as acne and/or seborrhea and/or hirsutism and/or androgenic alopecia. The invention also concerns a method for treating the scalp comprising application on the scalp of a compn. contg., in a physiol. acceptable medium, said DHEA deriv. Examples of a cream and lotion formulation contg. 7.alpha.-OH-DHEA and prepd. by std. methods are given.
IT **566-19-8**
RL: COS (Cosmetic use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cosmetic hair and skin prepns. contg. hydroxy-DHEA or keto-DHEA)
RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)

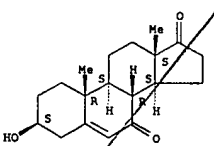
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:428719 CAPLUS
DOCUMENT NUMBER: 137:967
TITLE: Treatment of chronic fatigue syndrome and fibromyalgia syndrome with .DELTA.5-androsten-3.beta.-ol-7,17-dione and metabolizable precursors
INVENTOR(S): Zenk, Ronald J.; Zenk, John L.
PATENT ASSIGNEE(S): Humanetics Corporation, USA
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002043737	A1	20020606	WO 2001-US46241	20011031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-250227P P 20001130
AB Chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS) can be treated by the administration of .DELTA.5-androsten-3.beta.-ol-7,17-dione and metabolizable precursors thereof.
IT **566-19-8** **566-19-8D**, metabolizable precursors
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treatment of chronic fatigue syndrome and fibromyalgia syndrome with .DELTA.5-androsten-3.beta.-ol-7,17-dione and metabolizable precursors)
RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

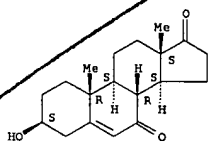
Absolute stereochemistry. Rotation (-).



RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L7 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



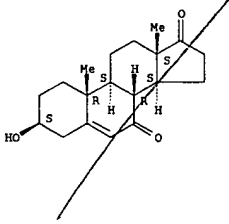
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:271056 CAPLUS
DOCUMENT NUMBER: 136:299719
TITLE: Dietary supplement for promoting healthy hormonal balance
INVENTOR(S): Hastings, Carl W.; Barnes, David J.; Daley, Christine A.
PATENT ASSIGNEE(S): Reliv' International, Inc., USA
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6368617	B1	20020409	US 2001-858047	20010515

AB A dietary supplement for promoting healthy hormonal balance in adult human subjects, and esp. in elderly subjects, comprises a secretagogue for stimulating the release of human growth hormone (hGH) by the pituitary, and the conversion by hGH to insulin-like growth factor 1 (IGF-1), in combination with 7-keto-dehydroepiandrosterone (7-keto DHEA). The dietary supplement also includes other interacting ingredients for delivering antioxidants for retarding damage at the cellular level caused by the presence of free radicals, and natural herbs for promoting physiol. health. For example, an essentially dry powder constituting a dietary supplement of this invention, to be dissolved in water to provide a daily serving, contained 7-keto-DHEA 25 mg, Symbiotropin 1000 mg, lecithin 200 mg, maltodextrin 7.227 mg, citric acid 640 mg, dipotassium phosphate 25 mg, potassium citrate 25 mg, probiotic blend 100 mg, fructo-oligosaccharides 400 mg, S-adenosyl-L-methionine 5 mg, acetyl-L-carnitine 100 mg, omega-3 fatty acids (Dry n-3) 125 mg, trimethylglycine 100 mg, coenzyme Q10 7.5 mg, resveratrol (Protykin) 10 mg, .alpha.-lipoic acid 50 mg, L-glutathione 30 mg, N-acetylcysteine 200 mg, and flavoring agents 300 mg.
IT **566-19-8**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(dietary supplement for stimulating release of human growth hormone and promoting healthy hormonal balance in humans)
RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L7 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

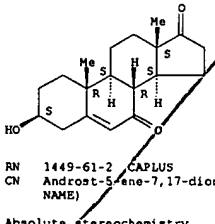
L7 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:240572 CAPLUS
DOCUMENT NUMBER: 136:257756
TITLE: Treatment of inflammatory bowel disease by the administration of .DELTA.5-androstene-3.beta.-ol-7,17 dione and metabolizable precursors thereof
INVENTOR(S): Zenk, Ronald J.; Zenk, John L.
PATENT ASSIGNEE(S): Humanetics Corporation, USA
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024205	A1	20020328	WO 2001-US28895	20010918

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-665640 A 20000919
AB Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease, can be treated by the administration of .DELTA.5-androstene-3.beta.-ol-7,17 dione and metabolizable precursors thereof.
IT **566-19-8 1449-61-2**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treatment of inflammatory bowel disease by the administration of .DELTA.5-androstene-3.beta.-ol-7,17 dione and metabolizable precursors)
RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

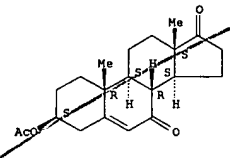
Absolute stereochemistry. Rotation (-).



RN 1449-61-2 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:617830 CAPLUS
DOCUMENT NUMBER: 135:190840
TITLE: Treatment of acute neuronal degeneration with 7.alpha.-hydroxy- derivatives of estradiols, dehydroepiandrosterones, pregnenolones and their metabolic precursors
INVENTOR(S): Lathe, Richard Frank; Seckl, Jonathan Robert; Martin, Keith Frank; Wulfert, Ernest Arne
PATENT ASSIGNEE(S): Hunter-Fleming Limited, UK; University of Edinburgh; BTG International Limited
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

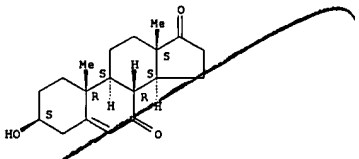
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060375	A2	20010823	WO 2001-GB627	20010215
WO 2001060375	A3	20020404		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-3524 A 20000215
OTHER SOURCE(S): MARPAT 135:190840
AB A method is provided for treating a patient in need of therapy for acute neuronal degeneration due to metabolic compromise of central or peripheral nervous system cells comprising administering to that patient a therapeutically effective amt. of a 7.alpha.-hydroxy substituted steroid selected from 7.alpha.-hydroxy-derivs. of estradiols, dehydroepiandrosterones and pregnenolones, and metabolic precursors thereof. Use of such compds. for manuf. of medicaments and neuroprotective compns. are also provided.
IT **566-19-8 566-19-8D**, 3-acyloxy esters
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treatment of acute neuronal degeneration with 7.alpha.-hydroxy-derivs. of estradiols, dehydroepiandrosterones, pregnenolones and their metabolic precursors)
RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

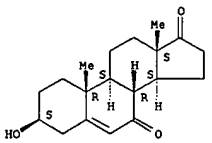
Absolute stereochemistry. Rotation (-).

L7 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

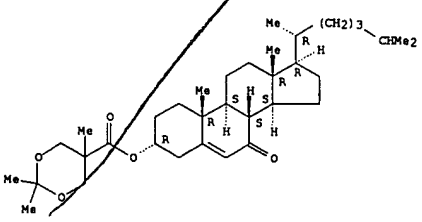


L7 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:488533 CAPLUS
DOCUMENT NUMBER: 135:92780
TITLE: Synthesis of steroidal derivatives as lipoprotein biosynthesis inhibitors
INVENTOR(S): Brumby, Thomas; Halfbrodt, Wolfgang; Jaroch, Stefan; Mueller, Hans-joachim; Schoellkopf, Klaus; Heck, Reinhard
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 76 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19963266	A1	20010705	DE 1999-19963266	19991216

OTHER SOURCE(S): MARPAT 135:92780
AB Steroidal derivs., such as I [R1 = H, CH2S-alkyl, CH2NHCOPh, .alpha.-CH2NHCO2CH2Ph; R1R2 = CH(OH); R1R3 = (un)substituted oxazinone ring, pyrazole ring; R2 = H; R2R4 = bond; R3 = H, OH, OCONH2, NH2, NH-alkyl, N(alkyl)2; R3R4 = O; R4 = H, CO2H, CONH2, CF3, etc.; R5 = H, OH; R5R6 = O, CH(OH), 4-carbon ring; oxygen contg. C3-6-ring; R5R7 = double bond; R6 = H, hydroxy substituted C2-8-alkenyl, C1-8-alkyl-S-alkyl; R7 = H, CH2NO2; R7R8, R7R9 = double bond; R8 = H, OH, NHCO-alkyl; R9 = H, CH2S-alkyl, NHCOCMe(CH2OH)2, NHCO-(2,2,5-trimethyl-1,3-dioxolan-5-yl); R10 = H; R10R11 = O; R11 = H; R11R12 = double bond; R12 = H; R13 = H, Et; X = O, NH, N-alkyl,CH2,CH(OH),CH(CH2S-alkyl), C(OH)(CH2S-alkyl); XR3 = tetrazole], were prepd. in all optically active forms, as racemates, diastereomers and diastereomeric mixts. for use as lipoprotein [Lp(a)] biosynthesis inhibitors. Thus, cholestane deriv. II was prepd. via a multistep synthetic sequence starting from cholest-4-en-3-one.
IT **348609-84-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cholestane derivs. as lipoprotein biosynthesis inhibitors)
RN 348609-84-7 CAPLUS
CN Cholest-5-en-7-one, 3-[[(2,2,5-trimethyl-1,3-dioxan-5-yl)carbonyl]oxy]-, (3.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

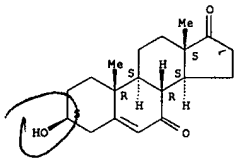
L7 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:287544 CAPLUS
DOCUMENT NUMBER: 134:348389
TITLE: Effects of transdermal application of 7-oxo-DHEA on the levels of steroid hormones, gonadotropins and lipids in healthy men
AUTHOR(S): Sulcova, J.; Hill, M.; Masek, Z.; Ceska, R.; Novacek, A.; Hampl, R.; Starka, L.
CORPORATE SOURCE: Institute of Endocrinology, First Faculty of Medicine, Charles University, Prague, Czech Rep.
SOURCE: Physiological Research (Prague) (2001), 50(1), 9-18
CODEN: PHRSEJ; ISSN: 0862-8408
PUBLISHER: Institute of Physiology, Academy of Sciences of the Czech Republic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to investigate the effect of 7-oxo-DHEA (dehydroepiandrosterone) on the serum levels of steroid sexual hormones, gonadotropins, lipids and lipoproteins in men. 7-Oxo-DHEA was applied onto the skin as a gel to 10 volunteers aged 27 to 72 yr for 5 consecutive days. The single dose contained 25 mg 7-oxo-DHEA. Serum concns. of testosterone, estradiol, cortisol, androstenedione, LH, FSH, sex hormone binding globulin (SHBG), total cholesterol, HDL- and LDL-cholesterol, triglycerides, apolipoprotein A-I and B and lipoprotein(a) were measured before the beginning and shortly after the end of the steroid application. After the treatment, the authors noted the following significant changes: a decline of testosterone and estradiol levels, increase of LH, HDL-cholesterol and apolipoprotein A-I levels. The decrease of total cholesterol levels was of the borderline significance. A slight but significant increase was found in apolipoprotein B and lipoprotein(a). The most expressive was the fall of the atherogenic index. The authors suggest that the gel contg. 7-oxo-DHEA might be a suitable drug for improving the compn. of the steroid and lipid parameters in elderly men.

IT **566-19-8**, 7-Oxo-dehydroepiandrosterone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(transdermal application of oxo-DHEA effect on blood steroid hormones, gonadotropins and lipids in healthy men)

RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS

L7 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:247354 CAPLUS
DOCUMENT NUMBER: 134:261560
TITLE: Therapeutic treatment of androgen receptor driven conditions using steroids or analogs
INVENTOR(S): Lardy, Henry A.; Marwah, Padma
PATENT ASSIGNEE(S): Hollis-Eden Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023405	A2	20010405	WO 2000-US26848	20000928
WO 2001023405	A3	20020530		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000077363	A5	20010430	AU 2000-77363	20000928
EP 1228083	A2	20020807	EP 2000-967114	20000928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MX, CY, AL				

PRIORITY APPLN. INFO.: US 1999-157275P P 19990930
US 1999-157347P P 19990930
US 1999-166116P P 19991116
WO 2000-US26848 W 20000928

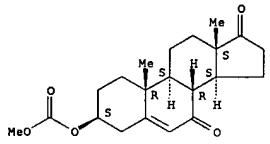
OTHER SOURCE(S): MARPAT 134:261560

AB A method is claimed to treat or prevent an androgen responsive disease in a subject, or to ameliorate one or more symptoms thereof, comprising administering to a subject, or delivering to the subject's tissues, an effective amt. of a steroid or steroid analogs. The steroid is specifically an analog of 1,3,5(10)-estratriene-17.alpha.-ethynyl-3.beta.,17.beta.-diol; 17.alpha.-ethynylandrostene-3.beta.,17.beta.-diol; 3.beta.,17.beta.-dihydroxyandrost-5-en-16-one; or 3.beta.-methylcarbonate-androst-5-en-7,17-dione. The androgen responsive disease is prostate cancer, benign prostatic hyperplasia, breast cancer, alopecia, acne, hypogonadism or hirsutism. The method further comprises administering to the subject a second therapy, the second therapeutic agent is hydroxyflutamide, leuprolide, megesterol, diethylstilbesterol, aminoglutethimide, spironolactone, tamoxifen, cyproterone acetate, or bicalutamide.

IT **250163-05-4DP**, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic treatment of androgen receptor driven conditions using steroids or analogs)

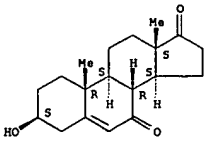
RN 250163-05-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-[(methoxycarbonyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

L7 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)
Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:820640 CAPLUS
DOCUMENT NUMBER: 134:95631
TITLE: Safety and pharmacokinetic study with escalating doses of 3-acetyl-7-oxo-dehydroepiandrosterone in healthy male volunteers
AUTHOR(S): Davidson, Michael; Marwah, Ashok; Sawchuk, Ronald J.; Maki, Kevin; Marwah, Padma; Weeks, Charles; Lardy, Henry
CORPORATE SOURCE: Chicago Center for Clinical Research, Chicago, IL, USA
SOURCE: Clinical and Investigative Medicine (2000), 23(5), 300-310
CODEN: CNVMDL; ISSN: 0147-958X
PUBLISHER: Canadian Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English

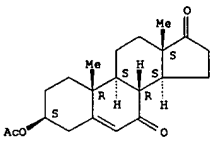
AB Studies were carried out to evaluate the safety and pharmacokinetics of 3-acetyl-7-oxo-DHEA (3.beta.-acetoxyandrost-5-ene-7,17-dione) given orally. The study consisted of a randomized, double blind, placebo-controlled, escalating dose study in the Chicago Center for Clin. Research involving 22 healthy men. The participants received placebo or 3-acetyl-7-oxo-DHEA at 50 mg/d for 7 days followed by a 7-day washout; 100 mg/d for 7 days followed by a 7-day washout; and 200 mg/d for 28 days. Safety parameters, evaluated at each dose level, included measurement of total testosterone, free testosterone, dihydrotestosterone, estradiol, cortisol, thyroxine and insulin levels. Analyses for 7-oxo-DHEA-3.beta.-sulfate (DHEA-S), the only detectable metabolic product of the administered steroid, were conducted on plasma drawn from all subjects at 0.25, 0.5, 1, 2, 4, 6 and 12 h after the final 100 mg dose of 3.beta.-acetyl-7-oxo-DHEA. There were no differences in the clin. lab. values or in reported minor adverse experiences, between treatment and placebo groups. In general, blood hormone concns. were unaffected by the treatment with 3.beta.-acetyl-7-oxo-DHEA and remained within the normal range. No changes in vital signs, blood chem. or urinalysis occurred during treatment with 3.beta.-acetyl-7-oxo-DHEA compared to placebo. The administered steroid was not detected in the blood but was rapidly converted to 7-oxo-DHEA-S, the concns. of which were proportional to dose. This steroid sulfate did not accumulate; plasma concns. 12 h after the 3.beta.-acetyl-7-oxo-DHEA dose at 7 and 28 days on the 200 mg/d dose were 15.8 and 16.3 .mu.g/L resp. The mean time to peak plasma level of 7-oxo-DHEA-S was 2.2 h; the mean half life was 2.17 h. The apparent clearance averaged 172 L/h, and the apparent mean vol. of distribution was 540 L. These results indicate that 3.beta.-acetyl-7-oxo-DHEA is safe and well tolerated in normal healthy men at doses up to 200 mg/d for 4 wk.

IT **1449-61-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(dehydroepiandrosterone acetyloxo derive safety and pharmacokinetics and metab. and endocrine effects in men)

RN 1449-61-2 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:598290 CAPLUS
DOCUMENT NUMBER: 133:317704
TITLE: A randomized, double-blind, placebo-controlled study of 3-acetyl-7-oxo-dehydroepiandrosterone in healthy overweight adults
AUTHOR(S): Kalman, Douglas S.; Colker, Carlon M.; Swain, Melissa A.; Torina, Georgeann C.; Shi, Qiuhu
CORPORATE SOURCE: Peak Wellness, Inc., Greenwich, CT, 06830, USA
SOURCE: Current Therapeutic Research (2000), 61(7), 435-442
CODEN: CTCEA9; ISSN: 0011-393X
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to det. the effects of 3-acetyl-7-oxo-dehydroepiandrosterone (7-oxo-DHEA) in healthy overweight adults. In a double-blind, placebo-controlled protocol, 30 adults (28 women and 2 men; mean age, 44.5 yr) with a mean body mass index of 31.9 kg/M2 were randomly divided into 2 groups of 15: Group 1 received 7-oxo-DHEA 100 mg twice daily and Group 2 received placebo for 8 wk. All subjects participated in an exercise training program 3 times per wk. Each exercise session consisted of 60 min of cross-training (aerobic and anaerobic exercise) under the supervision of an exercise physiologist. In addn., each subject was instructed to follow a diet of .apprx.1800 kcal/d (20 kcal/[kg/d]) by a registered dietitian. Subjects received biweekly dietary counseling to encourage compliance. Study participants underwent serum multiple-assay chem. testing, as well as body compn., blood pressure, and dietary anal. at baseline, week 4, and week 8. Of the 30 subjects who entered the study, 23 completed the 8-wk protocol. Seven subjects dropped out for personal reasons unrelated to the study. Group 1 lost a significant amt. of body wt. compared with Group 2 (-2.88 kg vs -0.97 kg) over the 8 wk. Group 1 also achieved a significant redn. in body fat compared with Group 2 (-1.8% vs -0.57%). The rate of change in body fat per 4-wk interval in Group 1 was 3.1 times that in Group 2 (-0.88% vs -0.28%). Group 1 also experienced a significant increase in triiodothyronine (T3) levels compared with Group 2 over the 8-wk study period (+17.88 ng/dL vs. 75 ng/dL). There were no significant changes in levels of TSH or thyroxine (T4) in either group. In addn., no significant changes were obsd. in vital signs, blood sugar, testosterone and estradiol levels, liver and renal function, or overall caloric intake during the study. No subjective adverse effects were reported throughout the study. The results of the study suggest that 7-oxo-DHEA combined with moderate exercise and a reduced-calorie diet significantly reduces body wt. and body fat compared with exercise and a reduced-calorie diet alone. In addn., 7-oxo-DHEA significantly elevated T3 levels but did not affect TSH or T4 levels, indicating that it does not adversely affect thyroid function in the short term.

IT **1449-61-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(dehydroepiandrosterone analog, exercise and dietary restriction effect on body wt. and compn., thyroid function, sex hormones and other physiol. parameters in healthy overwt. humans)

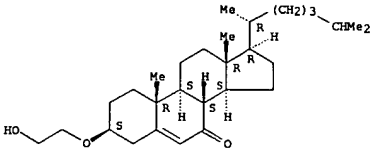
RN 1449-61-2 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:243977 CAPLUS
DOCUMENT NUMBER: 133:114584
TITLE: Structure-apoptotic potency evaluations of novel sterols using human leukemic cells
AUTHOR(S): Johnson, Betty H.; Russell, Michael J.; Krylov, Alexander S.; Medh, Rheem D.; Ayala-Torres, Sylvette; Regner, Justin Lee; Thompson, E. Brad
CORPORATE SOURCE: Department of Human Biological Chemistry and Genetics, The University of Texas Medical Branch, Galveston, TX, 77555-0645, USA
SOURCE: Lipids (2000), 35(3), 305-315
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three oxidized analogs of cholesterol have been characterized for their ability to cause apoptotic cell death in CEM-C7-14 human leukemic cells. In addn. to testing 15-ketocholestenol (K15), 15-ketocholestenol hydroxyethyl ether (CK15), and 7-ketocholesterol hydroxyethyl ether (CK7), an oxysterol of known apoptotic response, 25-hydroxycholesterol (25OHC), served as a std. for comparison. Growth studies based on dye exclusion by viable cells while using a sublethal concn. of oxysterols ranked their potency for cell killing as 25OHC > K15 > CK15 > CK7. Both the TUNEL assay (terminal deoxynucleotidyl transferase-mediated dUTP-X nick end labeling), which quantifies the amt. of DNA nicks caused by a toxic agent, and the MTT assay, which measures cell metab. and thus reflects cell viability, substantiated the same rank order. An ELISA assay for evaluating release of DNA fragments into the cytosol after treatment gave a similar potency order. The oncogene c-myc mRNA was suppressed by all three oxysterols, with 25OHC and K15 being the most potent suppressors. Hoechst and Annexin V staining documented that these oxysterols kill cells by an apoptotic pathway as evidenced by condensation of nuclear chromatin and plasma membrane inversion, resp. From these in vitro studies, we believe that 25OHC, K15, and possibly CK15 have the potential to be chemotherapeutic agents.

IT **155252-30-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(structure-apoptotic potency evaluations of novel sterols using human leukemic cells)

RN 155252-30-5 CAPLUS
CN Cholest-5-en-7-one, 3-(2-hydroxyethoxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 17 OF 41 CAPLUS COPYRIGHT 2002 ACS

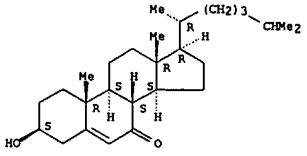
ACCESSION NUMBER: 2000:237584 CAPLUS
DOCUMENT NUMBER: 133:125256
TITLE: Analysis of 7-ketocholesterol in low density lipoprotein and fatty acid composition in erythrocyte membranes of patients on maintenance hemodialysis and healthy controls
AUTHOR(S): Tsuzuki, D.; Sumino, K.; Yokoyama, M.
CORPORATE SOURCE: Department of Public Health, Kobe University, School of Medicine, Kobe, Hyogo, Japan
SOURCE: Clinica Chimica Acta (2000), 295(1-2), 155-168
CODEN: CCATAR; ISSN: 0009-8981
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We established a method to quantify 7-ketocholesterol (7-KC) in low d. lipoprotein by using the heparin-citrate method and gas chromatog.-mass spectrometry. We examd. the concn. of 7-ketocholesterol in LDL using this method to assess the pathol. conditions in uremic patients with hemodialysis and healthy controls. We also examd. the fatty acid compn. in erythrocyte membranes to est. the modification of biol. membranes. We showed that the concns. of 7-KC/cholesterol in LDL were significantly increased in hemodialysis patients compared to healthy controls (3.68.+-.0.45 vs. 2.41.+-.0.19, P<0.05) and the ratio of polyunsatd. fatty acids to satd. fatty acids in erythrocyte membranes was significantly decreased in hemodialysis patients compared to healthy controls (0.499.+-.0.014 vs. 0.655.+-.0.017, P<0.001). There was no significant difference in 7-KC concn. in LDL or fatty acid compn. in erythrocyte membranes between pre- and post-intervention of hemodialysis. We concluded that hemodialysis patients are under oxidative stress, which modifies LDL and erythrocyte membranes and we speculated these modifications may participate in the process of atherosclerosis. We believe that the method to quantify 7-KC in this study is concise and reliable and may be used to investigate various diseases.

IT **566-28-9**, 7-Ketocholesterol
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(anal. of 7-ketocholesterol in LDL and fatty acid compn. in erythrocyte membranes of patients on maintenance hemodialysis and healthy controls)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)

L7 ANSWER 18 OF 41 CAPLUS COPYRIGHT 2002 ACS

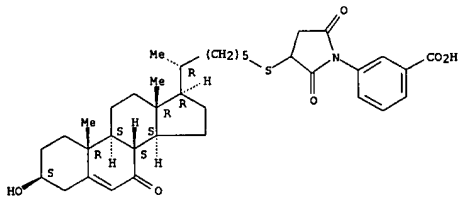
ACCESSION NUMBER: 2000:51386 CAPLUS
DOCUMENT NUMBER: 132:262320
TITLE: Utility of i-steroid-route to oxidized sterol bound to a cross-linker: synthesis of the steroid antigen
AUTHOR(S): Kim, Byung Ju; Morita, Hiroyuki
CORPORATE SOURCE: Department of System Engineering of Materials and Life Science, Faculty of Engineering, Toyama University, Toyama, 930-8555, Japan
SOURCE: Chemistry Letters (2000), (1), 42-43
CODEN: CMLTAG; ISSN: 0366-7022
PUBLISHER: Chemical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The target sterol, which was for prepn. of oxidized sterol antigen to apply to a new antibody diagnostic method for circulatory disease, was successfully synthesized via i-steroid transformation as followings: (1) the Grignard reaction, (2) Barton-McCombie reaction, (3) regioselective photolytic-addn. of thiolacetic acid toward 25-double bond, and (4) in situ Michael addn. between the thiol and a cross-linker.

IT **263356-67-8DP**, conjugate with keyhole limpet protein
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(utility of i-steroid-route to oxidized sterol bound to a cross-linker for the synthesis of steroid antigen)

RN 263356-67-8 CAPLUS
CN Benzoic acid, 3-[3-[[(3.beta.)-3-hydroxy-7-oxo-27-norcholest-5-en-26-yl]thio]-2,5-dioxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:684497 CAPLUS
DOCUMENT NUMBER: 131:332293
TITLE: Suppression of .DELTA.5-androstenediol-induced androgen receptor transactivation by selective steroids in human prostate cancer cells
AUTHOR(S): Chang, Hong-Chiang; Miyamoto, Hiroshi; Marwah, Padma; Lardy, Henry; Yeh, Shuyuan; Huang, Ko-En; Chang, Chawnshang
CORPORATE SOURCE: George Whipple Laboratory for Cancer Research, Departments of Pathology, Urology, Radiation Oncology, and the Cancer Center, University of Rochester Medical Center, Rochester, NY, 14642, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(20), 11173-11177
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

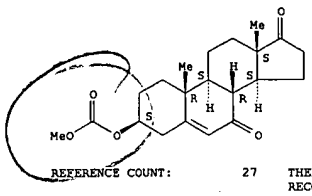
AB The authors' earlier report suggested that androst-5-ene-3.beta.,7.beta.-diol (.DELTA.5-androstenediol or Adiol) is a natural hormone with androgenic activity and that two potent anti-androgens, hydroxyflutamide (Eulexin) and bicalutamide (Casodex), fail to block completely the Adiol-induced androgen receptor (AR) transactivation in prostate cancer cells. Here, the authors report the development of a reporter assay to screen several selective steroids with anti-Adiol activity. Among 22 derivs./metabolites of dehydroepiandrosterone, the authors found 4 steroids [no. 4, 1,3,5(10)-estratriene-17.alpha.-ethynyl-3,17.beta.-diol; no. 6, 17.alpha.-ethynyl-androstene-diol; no. 8, 3.beta.,17.beta.-dihydroxy-androst-5-ene-16-one; and no. 10, 3.beta.-methylcarbonate-androst-5-ene-7,17-dione] that have no androgenic activity and could also block the Adiol-induced AR transactivation in prostate cancer PC-3 cells. Interestingly, these compds., in combination with hydroxyflutamide, further suppressed the Adiol-induced AR transactivation. Reporter assays further showed that these four anti-Adiol steroids have relatively lower glucocorticoid, progesterone, and estrogenic activity. Together, these data suggest some selective steroids might have anti-Adiol activity, which may have potential clin. application in the battle against the androgen-dependent prostate cancer growth.

IT **250163-05-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(androstenediol-induced androgen receptor transactivation suppression by selective steroids in human prostate cancer cells)

RN 250163-05-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-[(methoxycarbonyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)

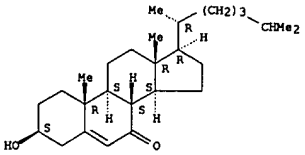


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:433949 CAPLUS
DOCUMENT NUMBER: 127:117127
TITLE: Evaluation of the cytotoxic effects of some oxysterols and of cholesterol on endothelial cell growth: methodological aspects
AUTHOR(S): Lizard, G.; Gueldry, S.; Deckert, V.; Gambert, P.; Lagrost, L.
CORPORATE SOURCE: INSERM-CJF 93/10, Laboratoire de Biochimie Medicale, Hopital de Bocage, Dijon, 21034, Fr.
SOURCE: Pathologie Biologie (1997), 45(4), 281-290
CODEN: PTBIAN; ISSN: 0031-3009
PUBLISHER: Expansion Scientifique Francaise
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of various oxysterol (7.beta.-hydroxycholesterol, 7-ketocholesterol, 19-hydroxycholesterol, cholesterol-5.alpha.,6.alpha.-epoxide, and 25-hydroxycholesterol) and of cholesterol were investigated on cell growth of bovine aortic endothelial (BAE) cells by cell counting, MTT redn., and 3H-thymidine incorporation in a 5 to 80 .mu.g/mL concn. range. By cell counting, a dose related decrease in the no. of adherent cells was obsd. with oxysterols; MTT redn. also indicated a decreased no. of viable cells, and both method give similar IC50. A lower 3H-thymidine incorporation was generally detected with oxysterols but no effect on 3H-thymidine incorporation was found with 25-hydroxycholesterol. With cholesterol, no modification of cell growth was shown by cell counting and 3H-thymidine incorporation, whereas an important decrease in MTT redn. was obsd. Noteworthy, with the highest cholesterol concn. no change in cellular morphol. occurred, and no modification of mitochondrial activity was found with Rhodamine 123. It is concluded that MTT and 3H-thymidine incorporation are not suitable for the evaluation of a putative toxicity of cholesterol and 25-hydroxycholesterol, resp. Therefore, cell counting seems the most accurate method to det. the effects of oxysterols and of cholesterol and endothelial cell growth. The results are discussed in relation to the antiangiogenic activity of the oxysterols.
IT **566-28-9**, 7-Ketocholesterol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(evaluation of cytotoxic effects of oxysterols and of cholesterol on vascular endothelial cell growth in relation to methodol. aspects)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

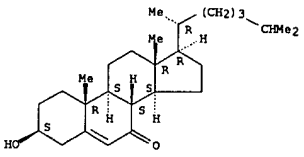
Absolute stereochemistry.

L7 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



L7 ANSWER 27 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:430012 CAPLUS
DOCUMENT NUMBER: 127:117125
TITLE: Isolation and structure identification of two constituents with antitumor activity from human fetal liver
AUTHOR(S): Zhang, Qinglin; Wu, Zhuze; Cao, Jurong; Feng, Rui; Du, Zehan
CORPORATE SOURCE: Inst. Radiation Med., Acad. Military Med. Sci., Beijing, 100850, Peop. Rep. China
SOURCE: Junshi Yixue Kexueyuan Yuankan (1996), 20(4), 266-268
CODEN: JYKYEL; ISSN: 1000-5501
PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB 2 Suppressors were sepd. and purified from methanol-acetone ext. of human fetal liver, with the isolation process guarded by suppression of HL-60 cells growth in vitro. The procedure for purifn. included C18 reversed-phase medium pressure chromatog., gel filtration on Sephadex LH-20, and HPLC. The suppressors were identified to be 7-ketocholesterol and 7.beta.-hydroxycholesterol by high resoln. MS and NMR, and both had more evident inhibitory effect on HL-60 cell proliferation than that of the hGM-CFU.
IT **566-28-9P**, 7-Ketocholesterol
RL: PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(isolation and structure identification of two constituents with antitumor activity from human fetal liver)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



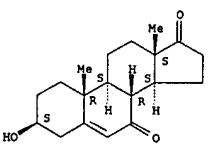
L7 ANSWER 28 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:9924 CAPLUS
DOCUMENT NUMBER: 126:113708
TITLE: Treatment of immune system with .DELTA.5-androstenes
INVENTOR(S): Lardy, Henry A.
PATENT ASSIGNEE(S): Humanetics Corporation, USA
SOURCE: U.S., 7 pp., Cont.-in-part of U.S. 5,292,730.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5585371	A	19961217	US 1994-189917	19940202
US 5296481	A	19940322	US 1992-867288	19920410
US 5292730	A	19940308	US 1992-922850	19920731
US 5424463	A	19950613	US 1994-327843	19941024
US 5506223	A	19960409	US 1994-327646	19941024
US 5807848	A	19980915	US 1996-771335	19961216
US 5707983	A	19980113	US 1997-806541	19970224

PRIORITY APPLN. INFO.: US 1990-575156 B1 19900829
US 1992-867288 A2 19920410
US 1992-922850 A2 19920731
US 1993-123151 B1 19930902
US 1994-189917 A2 19940202
US 1995-527746 A3 19950913

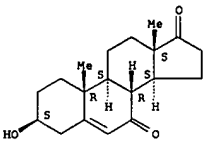
AB Immune system response may be enhanced by administering a .DELTA.5-Androsten-3.beta.-ol-17-one having a C7 substituent selected from the group consisting of oxo, hydroxy and groups convertible thereto by hydrolysis.
IT **566-19-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(treatment of immune system with .DELTA.5-androstenes)
RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



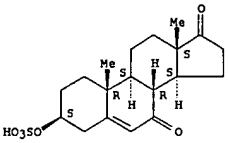
L7 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaccine compns. and method for induction of mucosal immune response via systemic vaccination)
RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



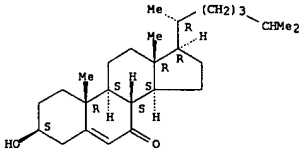
RN 4121-96-4 CAPLUS
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 32 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:250235 CAPLUS
DOCUMENT NUMBER: 124:332980
TITLE: Inhibitory effects of sterols isolated from Chlorella vulgaris on 12-O-tetradecanoylphorbol-13-acetate-induced inflammation and tumor promotion in mouse skin
AUTHOR(S): Yasukawa, Ken; Akihisa, Toshihiro; Kanno, Hiroshi; Kaminaga, Tomohiro; Izumida, Mitsuru; Sakoh, Takashi; Tamura, Toshitake; Takido, Michio
CORPORATE SOURCE: College of Pharmacy, Nihon University, Chiba, 274, Japan
SOURCE: Biol. Pharm. Bull. (1996), 19(4), 573-6
CODEN: BPBLEO; ISSN: 0918-6158
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Inhibitory activity against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice was obsd. in the methanol ext. of Chlorella vulgaris, a green alga. The hexane sol. fraction obtained from the methanol ext. exhibited marked inhibitory activity from which were isolated two .DELTA.5,7-sterols (ergosterol and 7-dehydroporiferasterol), two .DELTA.5,7,9(11)-sterols [9(11)-dehydroergosterol and 7,9(11)-bisdehydroporiferasterol], two 5.alpha.,8.alpha.-epidoxy-.DELTA.6-sterols (ergosterol peroxide and 7-dehydroporiferasterol peroxide), and a 7-oxo-.DELTA.5-sterol (7-oxocholesterol), among others. The .DELTA.5,7-sterols, 5.alpha.,8.alpha.-epidioxy-.DELTA.6-sterols and 7-oxo-.DELTA.5-sterol inhibited TPA-induced inflammation in mice. The 50% ID of these compds. for TPA-induced inflammation was 0.2-0.7 mg/ear. Furthermore, ergosterol peroxide markedly inhibited the tumor-promoting effect of TPA in 7,12-dimethylbenz[a]anthracene-initiated mice.
IT **566-28-9**, 7-Oxocholesterol
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitory effects of Chlorella vulgaris sterols on 12-O-tetradecanoylphorbol-13-acetate-induced inflammation and tumor promotion in mouse skin)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



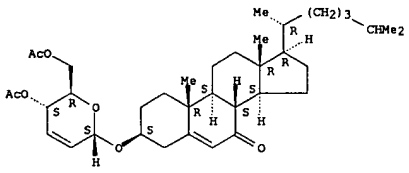
L7 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:181570 CAPLUS
DOCUMENT NUMBER: 124:233011
TITLE: Preparation of glycoside prodrugs with enhanced water solubility.
INVENTOR(S): Klemke, R.-Erich; Koreeda, Masato; Houston, Todd A.; Shull, Brian K.; Tuinman, Roeland J.
PATENT ASSIGNEE(S): Harrier, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532981	A1	19951207	WO 1995-US7027	19950601
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5693767	A	19971202	US 1994-251869	19940601
AU 9526617	A1	19951221	AU 1995-26617	19950601
PRIORITY APPLN. INFO.:			US 1994-251869 A	19940601
			US 1991-644002 A2	19910122
			US 1991-733915 B2	19910722
			US 1992-815691 B2	19920124
			US 1993-6447 B2	19930121
			WO 1995-US7027 W	19950601

AB Glycosides of aliph., alicyclic, aliph.-arom., and arom. aglycons having primary, secondary, or tertiary OH, SH, or CO2H groups with 2,3-dideoxy-.alpha.-D-erythrohex-2-enopyranoside fragments Q1-Q6 (A = acyl; X = O, S, CO2), were prepd. Thus, a mixt. of 4-acetamidophenol and hexaacetyl D-maltal was refluxed with iodine in THF for 12 h to give 30% of an .alpha.,.beta.-glycoside, which was stirred with Ba(OH)2 in MeOH to give glycoside (I). I had 8 times the H2O soly. of tylenol itself in phosphate-buffered saline at pH 7.4.
IT **136468-12-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glycoside prodrugs with enhanced water soly.)
RN 136468-12-7 CAPLUS
CN Cholest-5-en-7-one, 3-[(4,6-di-O-acetyl-2,3-dideoxy-.alpha.-D-erythro-hex-2-enopyranosyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



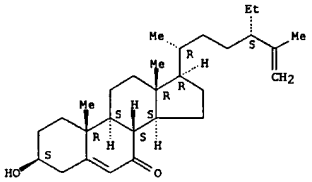
L7 ANSWER 34 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:1004432 CAPLUS
DOCUMENT NUMBER: 124:170093
TITLE: Oxygenated clerosterols isolated from the marine alga Codium arabicum
AUTHOR(S): Sheu, Jyh-Horng; Liaw, Chin-Chuang; Duh, Chang-Yih
CORPORATE SOURCE: Dep. Marine Resources, Natl. Sun Yat-Sen Univ., Kaohsiung, 804, Taiwan
SOURCE: Journal of Natural Products (1995), 58(10), 1521-6
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Society of Pharmacognosy
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Clerosterol, (24S)-24-ethyl-3-oxocholesta-4,25-dien-6.beta.-ol (I), (24S)-24-ethyl-5.alpha.-hydroperoxycholesta-6,25-dien-3.beta.-ol (II), (24S)-24-ethyl-7-oxocholesta-5,25-dien-3.beta.-ol (III), (24S)-24-ethyl-7.alpha.-hydroperoxycholesta-5,25-dien-3.beta.-ol (IV), and (24S)-24-ethylcholesta-5,25-dien-3.beta.,7.alpha.-diol (V), were isolated from the marine green alga Codium arabicum. A portion of steroid IV was epimerized to (24S)-24-ethyl-7.beta.-hydroperoxycholesta-5,25-dien-3.beta.-ol (VI). LiAlH4 redn. of an inseparable mixt. of IV and VI yielded diol V and (24S)-24-ethylcholesta-5,25-dien-3.beta.,7.beta.-diol (VII). Among these compds., sterols I, II, and IV were isolated for the 1st time from a natural source. Metabolites I-V showed significant cytotoxicity toward various cancer cell lines.

IT **173831-67-9P**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(oxygenated clerosterols isolated from Codium arabicum)

RN 173831-67-9 CAPLUS
CN Stigmasta-5,25-dien-7-one, 3-hydroxy-, (3.beta.,24S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:888257 CAPLUS
DOCUMENT NUMBER: 123:275418
TITLE: Lymphoma cells selected for resistance against the cytotoxic effect of oxygenated sterols are also resistant to nonsteroidal antiestrogens
AUTHOR(S): Low, Yoke L.; Hwang, Peter L. H.
CORPORATE SOURCE: Department of Physiology National University of Singapore, 10 Kent Ridge Crescent, Singapore, 0511, Singapore
SOURCE: Biochim. Biophys. Acta (1995), 1269(1), 32-40
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

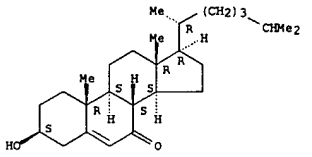
AB Oxygenated derivs. of cholesterol and related compds. (oxysterols) have long been known to be cytotoxic to many different cell types. The mechanism of this cytotoxic effect is not fully understood. The lab. has earlier reported that oxysterol cytotoxicity resembles that of nonsteroidal antiestrogens in some aspects: (i) the cytotoxic action of both types of compds. is blocked by inhibitors of protein or RNA synthesis, and (ii) both classes of compds. bind with high affinity to the microsomal antiestrogen binding site, a protein which may mediate the cytotoxicity of its ligands. The authors have now extended these studies by developing cell lines which are resistant to the cytotoxic action of oxysterols. Oxysterol-resistant cells were isolated by exposing 2 murine lymphoma cell lines, K36 and EL4, to incremental concns. of 7-ketocholestanol. Intriguingly, the resistant cells thus obtained also exhibited considerable resistance to the cytotoxic effects of nonsteroidal antiestrogens such as tamoxifen and clomiphene, having LD50 values which were 10-100-fold higher than that of the parental cells. The resistance appeared to be selective for oxysterols and antiestrogens and did not extend to non-specific toxic agents such as azide, ethanol, Triton X-100, or heat. The biochem. basis of the resistance is not clear but is not due to diminished cellular uptake or increased metab. of the cytotoxic agents or to changes in the antiestrogen-binding protein. The availability of the resistant cell lines should facilitate further studies on the mechanism of oxysterol- and antiestrogen-induced cell death.

IT **566-28-9**, 7-Ketocholesterol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lymphoma cells selected for resistance against cytotoxic effect of oxygenated sterols are also resistant to nonsteroidal antiestrogens)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



L7 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:693207 CAPLUS
DOCUMENT NUMBER: 123:83832
TITLE: .DELTA.5-androstenes useful for promoting weight maintenance or weight loss and treatment process
INVENTOR(S): Lardy, Henry A.; Reich, Ieva L.; Yong, Wei
PATENT ASSIGNEE(S): Humanetics Corp., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9506472	A1	19950309	WO 1994-US9852	19940901
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 08503491	T2	19940901	JP 1995-508253	19940901
CA 2148373	AA	19950309	CA 1994-2148373	19940901
AU 9476794	A1	19950322	AU 1994-76794	19940901
EP 666746	A1	19950816	EP 1994-927309	19940901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 202707	E	20010715	AT 1994-927309	19940901
ES 2160128	T3	20011101	ES 1994-927309	19940901
US 5424463	A	19950613	US 1994-327843	19941024
US 5506223	A	19960409	US 1994-327646	19941024

PRIORITY APPLN. INFO.: US 1993-123151 A 19930902
US 1990-575156 B1 19900829
US 1992-867288 A2 19920410
WO 1994-US9852 W 19940901

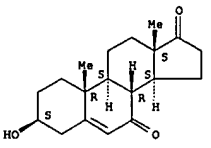
AB A method for promoting wt. control by treating a subject with a therapeutic amt. of one of .DELTA.5-androstene-3.beta.,7.alpha.-diol-17-one, .DELTA.5-androstene-3.beta.-ol-7,17-dione, .DELTA.5-androstene-3.beta.,7.alpha.,17.beta.-triol, .DELTA.5-androstene-3.beta.,17.beta.-diol-7-one, .DELTA.5-androstene-3.beta.-acetoxy-7,16,17-trione, .DELTA.5-androstene-3.beta.-16.alpha.-dihydroxy-7,17-dione, .DELTA.5-androstene-3.beta.-propionoxy-16.beta.-acetoxy-7,17-dione, .DELTA.5-androstene-3.beta.,7.alpha.,17.beta.-triol-16-one, .DELTA.5-androstene-3.beta.,17.beta.-diol-7,16-dione, .DELTA.5-androstene-3.beta.,16.alpha.,17.beta.-triol-7-one and derivs. thereof wherein one or more of the hydroxyl or keto substituents is a group convertible thereto by hydrolysis to stimulate wt. control without affecting appetite or inducing the synthesis of sex hormones. The steroids were prepd. by known methods.

IT **566-19-8P 2226-65-5P 109688-92-8P**
165181-82-8P 165181-86-2P 165181-89-5P
165181-93-1P 165181-95-3P
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .DELTA.5-androstenes useful for promoting wt. maintenance or wt. loss)

RN 566-19-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

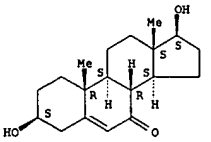
Absolute stereochemistry. Rotation (-).

L7 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



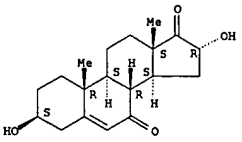
RN 2226-65-5 CAPLUS
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 109688-92-8 CAPLUS
CN Androst-5-ene-7,17-dione, 3,16-dihydroxy-, (3.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

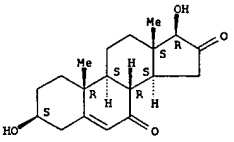
Absolute stereochemistry.



RN 165181-82-8 CAPLUS
CN Androst-5-ene-7,17-dione, 16-(phenylseleno)-3-[[(trimethylsilyl)acetyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

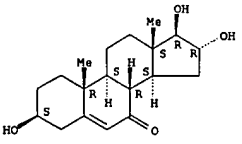
Absolute stereochemistry.

L7 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)

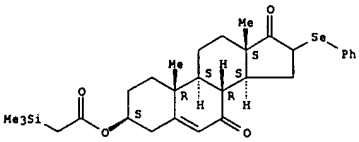


RN 165181-95-3 CAPLUS
CN Androst-5-en-17-one, 3,16,17-trihydroxy-, (3.beta.,16.alpha.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

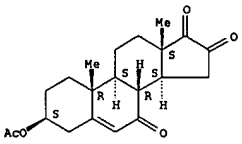


L7 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



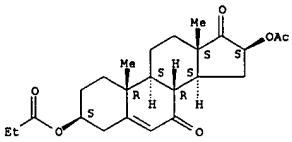
RN 165181-86-2 CAPLUS
CN Androst-5-ene-7,16,17-trione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 165181-89-5 CAPLUS
CN Androst-5-ene-7,17-dione, 16-(acetyloxy)-3-(1-oxopropoxy)-, (3.beta.,16.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 165181-93-1 CAPLUS
CN Androst-5-ene-7,16-dione, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 37 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:503245 CAPLUS
DOCUMENT NUMBER: 122:230779
TITLE: Use of sterols as anti-inflammatory agents
INVENTOR(S): Beneytout, Jean Louis; Andrianarison, Rivo Hery; Chambon, Serge
PATENT ASSIGNEE(S): Biodev, Fr.
SOURCE: Fr. Demande, 8 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

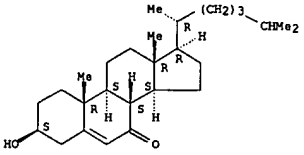
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2705030	A1	19941118	FR 1993-5665	19930511

AB Sterols such as cholesterol (I) or cholestane derivs. or precursors are useful as anti-inflammatory agents. A soln. contg. 100 .mu.M I acetate inhibited the activity of 12.mu.g lipoxygenase by 41%. Various pharmaceutical dosage forms are claimed.

IT **566-28-9**, 7-Oxo-cholesterol
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of sterols as anti-inflammatory agents)

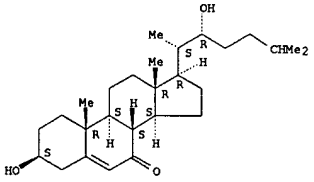
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L7 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:485816 CAPLUS
DOCUMENT NUMBER: 109:85816
TITLE: The 22- and 7,22-oxygenated cholesterols. Neoplastic growth inhibition and synergistic effect
AUTHOR(S): Stabursvik, Arnulv
CORPORATE SOURCE: Dep. Chem., Agric. Univ. Norway, As-Nlh, N-1432, Norway
SOURCE: Inst. Natl. Sante Rech. Med., [Colloq.] (1988), 166(Act. Biol. Oxysterols), 289-93
CODEN: CINMDE; ISSN: 0768-3154
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment of rats bearing dimethylbenzanthracene-induced mammary carcinomas with 7.beta.,22R-dihydroxycholesterol inhibited tumor growth and increased the life span. The in vitro effect of the 7-keto deriv. was comparable to that of the 7.beta.-OH compd., whereas the 7.alpha.-OH compd. was ineffective. Addn. of small amts. of 22R-hydroxycholesterol, which had no effect alone, doubled the antitumor effect of the 7.beta.-OH compd.
IT **104786-67-6**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neoplasm inhibition by, in mammary carcinoma)
RN 104786-67-6 CAPLUS
CN Cholest-5-en-7-one, 3,22-dihydroxy-, (3.beta.,22R)- (9CI) (CA INDEX NAME)

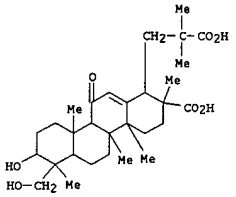
Absolute stereochemistry.



L7 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:627091 CAPLUS
DOCUMENT NUMBER: 105:227091
TITLE: Triterpene derivatives
INVENTOR(S): Furuta, Takuya; Kaise, Hirotsugu; Izawa, Taketoshi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 32 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

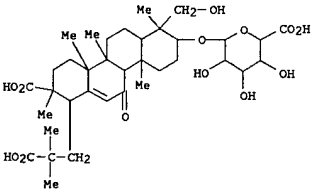
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61085344	A2	19860430	JP 1984-208990	19841003

AB The title compds. [I; R1 = OH, substituted alkoxy, Q, where R2 = H, acyl; R3 = H, alkyl; R4 = (substituted) HOCH2, CO2H; R1R4 = OCR5R6OCH2; R5, R6 = H, alkyl; Z = O, H2, (.alpha.-H, .beta.-OH); R7, R8 = CHO, CO2H, alkoxycarbonyl; R7R8 = CH2CO, substituted CH2CH2, (N-substituted) CH2NHCH2; X = bond, O] were prepd. Thus, oxidn. of I (R1 = OH; R4 = HOCH2; R7R8 = CH2CO; X = bond; Z = H2) with Ag2CO3, glycosidation of the resulting I (R4 = CHO) with Me 1-bromo-2,3,4-tri-O-acetyl-.beta.-D-glucopyranosiduronate, and oxidn. with Bu4NMnO4 at 40 .degree.C for 2 days gave I (R1 = Q, where R2 = Ac; R3 = Me; R4 = CO2H; R7R8 = CH2CO; X = bond; Z = H2). I showed anticomplement activity and inhibited blood platelet aggregation and are useful for the treatment and prevention of immune or autoimmune diseases, e.g., nephritis and collagenosis, and thrombosis (no data).
IT **105409-65-2P 105409-68-5P**
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as drug)
RN 105409-65-2 CAPLUS
CN 21,22-Secoolean-12-ene-21,22-dioic acid, 3,23-dihydroxy-11-oxo-, (3.beta.,4.beta.)- (9CI) (CA INDEX NAME)



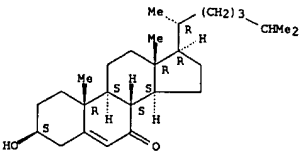
RN 105409-68-5 CAPLUS
CN 21,22-Secoolean-12-ene-21,22-dioic acid, 3-(.beta.-D-glucopyranuronosyloxy)-23-hydroxy-11-oxo-, (3.beta.,4.beta.)- (9CI) (CA

L7 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)
INDEX NAME)



L7 ANSWER 40 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:560958 CAPLUS
DOCUMENT NUMBER: 93:160958
TITLE: Hypocholesterolemic activity of phytosterol. II
AUTHOR(S): Tabata, Toshikazu; Tanaka, Mitsuo; Iio, Toshihiro
CORPORATE SOURCE: Showa Coll. Pharm. Sci., Tokyo, Japan
SOURCE: Yakugaku Zasshi (1980), 100(5), 546-52
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The hypocholesterolemic activities of phytosterols and related compds. were compared in rats receiving a 3% cholesterol [57-88-5]- contg. diet. The rats were i.v. injected for 5 days with emulsions of saline-albumin contg. each sterol. The greatest effect on lowering liver cholesterol, triglyceride, and fatty acid levels was shown by stigmasterol (I) [83-48-7], followed by .beta.-sitosterol [83-46-5], stigmastanol [83-45-4], ergosterol [57-87-4] and 7-ketocholesterol [566-28-9]. On the other hand, I palmitate [2308-84-1] and I stearate [23838-16-6] showed considerably lower activity than I. No effect could be seen in I acetate [4651-48-3], which is not found in nature. After injections, I in liver was present mainly in a free form and the palmitate or the stearate changed partly to the free form, 20% or 25% of the injected amt., resp. However, I acetate remained unchanged after injection. The cytochrome P-450 [9035-51-2] content of hepatic microsome from hypercholesterolemic rats was decreased by treatment with I and similar findings were obtained in microsomes from livers of normal or phenobarbital-treated rats which had been given I. The presence of a free hydroxy group at the C-3 position in phytosterols is apparently necessary for the hypocholesterolemic activities and a double bond at the C-5 position and a side-chain at the C-17 position, may also relate to these activities.
IT **566-28-9**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticholesteremic activity of, structure in relation to)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



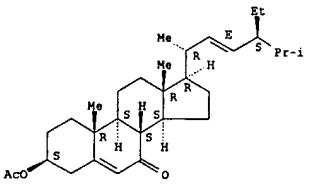
L7 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:198 CAPLUS
DOCUMENT NUMBER: 88:198
TITLE: Chemistry and biochemistry of Chinese drugs. Part II. Hydroxylated sterols, cytotoxic towards cancerous cells: synthesis and testing
AUTHOR(S): Nagano, Hajime; Poyser, J. Philip; Cheng, Kwok-Ping; Luu Bang; Ourisson, Guy; Beck, Jean Paul
CORPORATE SOURCE: Inst. Chim., Univ. Louis Pasteur, Strasbourg, Fr.
SOURCE: J. Chem. Res. (S) (1977), (9), 218
CODEN: JRPSDC
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cytotoxic activity was detd. of 23 cholesterol derivs. hydroxylated at C-1, -6, -7, -22, or -25, 20 cholesterol derivs. unsatd. in the side chain and hydroxylated at C-7, -20, -22, -23, or -24, 10 steroids hydroxylated at C-3 and carrying another O function, with varying side chain, and 5 tetracyclic triterpenes, esp. inotodiol derivs. The activity was measured against HTC and ZHC hepatoma cells and normal fibroblast 3T3 cells. Desmosterol derivs. were the most active and most selective. New compds. were prepd. by std. methods. In contrast to the report by A. N. Shivrina (1966), inotodiol is inactive.

IT **33028-07-8P 64907-23-9P 64907-26-2P 64933-64-8P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and cytotoxicity of)

RN 33028-07-8 CAPLUS
CN Stigmasta-5,22-dien-7-one, 3-(acetyloxy)-, (3.beta.,22E)- (9CI) (CA INDEX NAME)

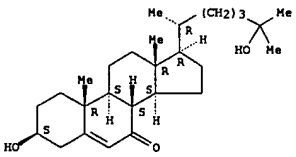
Absolute stereochemistry.
Double bond geometry as shown.



RN 64907-23-9 CAPLUS
CN Cholest-5-en-7-one, 3,25-dihydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

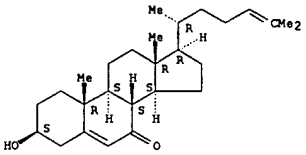
Absolute stereochemistry.

L7 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2002 ACS (Continued)



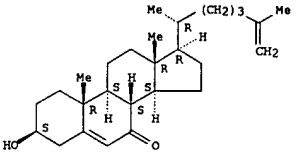
RN 64907-26-2 CAPLUS
CN Cholesta-5,24-dien-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 64933-64-8 CAPLUS
CN Cholesta-5,25-dien-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



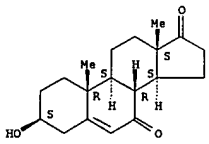
```
=> d his

     (FILE 'HOME' ENTERED AT 15:37:32 ON 19 AUG 2002)

     FILE 'REGISTRY' ENTERED AT 15:37:37 ON 19 AUG 2002
L1               STRUCTURE UPLOADED
L2             4 S L1
L3               STRUCTURE UPLOADED
L4             3 S L3
L5           627 S L3 FULL

     FILE 'CAPLUS' ENTERED AT 15:40:30 ON 19 AUG 2002
L6          1470 S L5
L7            41 S L5/THU

=> d ibib ab hitstr 1-75
```

L9 ANSWER 1 OF 75 USPATFULL
ACCESSION NUMBER: 2000:161003 USPATFULL
TITLE: Memory enhancement by the administration of .DELTA.5-androstene-3.beta.-ol-7,17-dione and 3.beta. esters thereof
INVENTOR(S): Lardy, Henry A., Madison, WI, United States
Shi, Jennifer Y., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, Chanhassen, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6153606		20001128
APPLICATION INFO.:	US 1998-174235		19981016 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rose, Shep K.
LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 217
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The memory of a healthy mammal and the memory of a mammal with age impaired memory can be improved by administering an effective amount of .DELTA.5-Androstene-3.beta.-ol-7,17-dione and 3.beta. esters thereof.
IT **566-19-8 566-19-8D**, 3.beta.-esters
(memory enhancement by administration of .DELTA.5-androstene-3.beta.-ol-7,17-dione and 3.beta. esters thereof)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

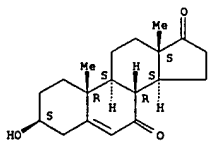
Absolute stereochemistry. Rotation (-).



RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L9 ANSWER 1 OF 75 USPATFULL (Continued)



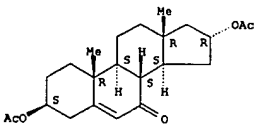
L9 ANSWER 2 OF 75 USPATFULL
ACCESSION NUMBER: 2000:150305 USPATFULL
TITLE: Process for the stereoselective synthesis of 16-substituted-4-aza-androstanones
INVENTOR(S): Gratale, Dominick F., Edison, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Sahoo, Soumya P., Old Bridge, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6143887		20001107
APPLICATION INFO.:	US 1999-309833		19990511 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-85449P	19980514 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rotman, Alan L.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 968
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The novel process of the present invention involves the stereoselective synthesis of certain 16.beta.-substituted 4-aza-5.alpha.-androstan-3-ones and the useful intermediates obtained therein.
IT **178061-76-2**
(stereoselective synthesis of 16-substituted aza-androstanones)
RN 178061-76-2 USPATFULL
CN Androst-5-en-7-one, 3,16-bis(acetyloxy)-, (3.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 3 OF 75 USPATFULL
ACCESSION NUMBER: 2000:150158 USPATFULL
TITLE: Therapeutic uses for an aminosterol compound
INVENTOR(S): Zasloff, Michael, Merion Station, PA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals, Inc., Plymouth, PA, United States (U.S. corporation)

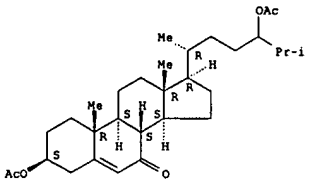
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6143738		20001107
APPLICATION INFO.:	US 1997-857288		19970516 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-487443, filed on 7 Jun 1995, now patented, Pat. No. US 5847172, issued on 8 Dec 1998		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-32378P	19961206 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Goldberg, Jerome D.
LEGAL REPRESENTATIVE: Morgan, Lewis & Bockius LLP
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 31 Drawing Figure(s); 25 Drawing Page(s)
LINE COUNT: 1002
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical composition includes, as an active ingredient, a compound according to formula 1436 as shown in FIG. 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient. Various pharmaceutical products may be produced including this pharmaceutical composition. Such pharmaceutical products may be used for the treatment of cancers, such as leukemia; inflammation; arthritis; and viruses, such as HSV. Methods for using the pharmaceutical compositions also are described. In these methods, various diseases are treated or other body functions are activated or inhibited by administering an effective amount of the pharmaceutical composition. For example, inflammation, arthritis, herpes simplex virus, melanoma, and leukemia may be treated by administering an effective amount of the pharmaceutical compositions. Viral replication, weight gain, and growth factor production can be inhibited by administering an effective amount of these pharmaceutical compositions. Appetite can be suppressed by administering an effective amount of the pharmaceutical compositions, and a diuretic effect can be produced.
IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 3 OF 75 USPATFULL (Continued)



L9 ANSWER 4 OF 75 USPATFULL

ACCESSION NUMBER: 2000:114144 USPATFULL
TITLE: Process for effecting allylic oxidation
INVENTOR(S): Marwah, Padma, Madison, WI, United States
Lardy, Henry A., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, St. Louis Park, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6111118		20000829
APPLICATION INFO.:	US 1999-228902		19990111 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-851939, filed on 7 May 1997, now patented, Pat. No. US 5869709		

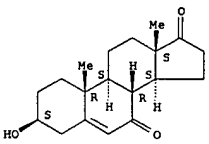
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose' G.
ASSISTANT EXAMINER: Pryor, Alton
LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
LINE COUNT: 1361
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A procedure for oxidizing organic compounds having allylic hydrogen atom(s) involving the steps of reactively contacting the organic compound with a combination of a periodic acid or metal periodate and an alkyl hydroperoxide under conditions of normal as well as elevated pressure of a suitable gas like air. The reaction can conveniently be conducted at temperatures between about 0-65.degree. C. in a cosolvent system of water and organic solvent(s).

IT **566-19-8P**, 3.beta.-Hydroxyandrost-5-ene-7,17-dione
809-51-8P, 7-Oxocholesteryl acetate **1449-61-2P**
13209-60-4P, 3.beta.,17.beta.-Diacetoxyandrost-5-en-7-one
(process for effecting allylic oxidn.)

RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

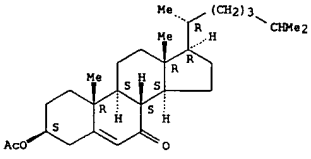
Absolute stereochemistry. Rotation (-).



RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

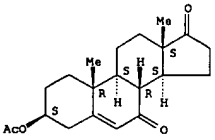
Absolute stereochemistry.

L9 ANSWER 4 OF 75 USPATFULL (Continued)



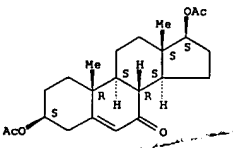
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 5 OF 75 USPATFULL

ACCESSION NUMBER: 2000:95104 USPATFULL
TITLE: Glycoside compounds and methods of synthesis
INVENTOR(S): Shull, Brian K., Durham, NC, United States
Tuinman, Roeland J., Yosilanti, MI, United States
Houston, Todd A., Glen Allen, VA, United States
Klemke, R. Erich, Hilzingen, Germany, Federal Republic of
Koreeda, Masato, Ann Arbor, MI, United States
PATENT ASSIGNEE(S): The Regents of the University of Michigan, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6093805		20000725
APPLICATION INFO.:	US 1997-915699		19970821 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-251869, filed on 1 Jun 1994, now patented, Pat. No. US 5693767, issued on 2 Dec 1997 which is a continuation-in-part of Ser. No. US 1993-6447, filed on 21 Jan 1993 which is a continuation-in-part of Ser. No. US 1992-815691, filed on 24 Jan 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-733915, filed on 22 Jul 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-644002, filed on 22 Jan 1991, now patented, Pat. No. US 5278296, issued on 11 Jan 1994		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lee, Howard C.
LEGAL REPRESENTATIVE: Medlen & Carroll, LLP
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1108
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

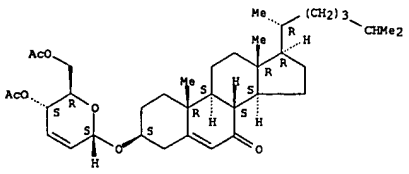
AB Novel glycosides, especially steroidal and non-steroidal glycosides are provided. The steroidal and non-steroidal glycosides preferably are prepared from aglycons which possess valuable properties such as pharmacological properties. The glycosides are prepared from useful aglycons and possess useful properties which are the same as those of their respective unglycosylated aglycons. The glycosides are provided in acylated and deacylated form. The acylated glycosides after hydrolysis of the acyl groups possess enhanced water solubility properties, as illustrated in the case where the aglycon is acetominophen.

IT **136468-12-7P**
(prepn. and redn. of)

RN 136468-12-7 USPATFULL
CN Cholest-5-en-7-one, 3-[(4,6-di-O-acetyl-2,3-dideoxy-.alpha.-D-erythro-hex-2-enopyranosyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 5 OF 75 USPATFULL (Continued)



L9 ANSWER 6 OF 75 USPATFULL

ACCESSION NUMBER: 2000:60853 USPATFULL
TITLE: Portable alarm apparatus for sudden heart attack patient
INVENTOR(S): Li, Pao-Lang, 532, Min-Tzwu Rd. Lu Chou Hsiang, Taipei, Taiwan, Province of China

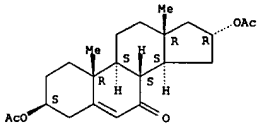
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6063036		20000516
APPLICATION INFO.:	US 1998-85449		19980528 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-25798, filed on 19 Feb 1998		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: O'Connor, Cary
ASSISTANT EXAMINER: Astorino, Michael
LEGAL REPRESENTATIVE: Rosenberg, Klein & Lee
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 169
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A portable alarm apparatus for use by a sudden heart attack patient is provided that is characterized by a housing part connected to a suspension member for hanging around a patient's neck. Sensors are disposed on the suspension member and connected to an extending lead, enabling the sensors to contact respective pulse spots on the patient's neck, due to the downward force resulting from gravity acting on the housing part. The sensors detect the pulse signals in an artery in the user's neck corresponding to heartbeats and output an electrical signal for input to a control circuit disposed in the housing part for storage, display and generation of a warning alarm.

IT 178061-76-2
(stereoselective synthesis of 16-substituted aza-androstanones)
RN 178061-76-2 USPATFULL
CN Androst-5-en-7-one, 3,16-bis(acetyloxy)-, (3.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 7 OF 75 USPATFULL

ACCESSION NUMBER: 2000:41030 USPATFULL
TITLE: 6,7-oxygenated steroids and uses related thereto
INVENTOR(S): Burgoyne, David L., Delta, Canada
Shen, Yaping, Port Coquitlam, Canada
Langlands, John M., Richmond, Canada
Rogers, Christine, Vancouver, Canada
Chau, Joseph H.-L., Vancouver, Canada
Piers, Edward, Richmond, Canada
Salari, Hassan, Tswassen, Canada
PATENT ASSIGNEE(S): Inflazyme Pharmaceuticals Ltd., Richmond, Canada (non-U.S. corporation)
The University of British Columbia, Vancouver, Canada (non-U.S. corporation)
The University of Alberta, Alberta, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6046185		20000404
APPLICATION INFO.:	US 1997-893575		19970710 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1996-679642, filed on 12 Jul 1996, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-23450P	19960711 (60)

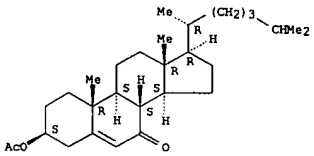
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose' G.
ASSISTANT EXAMINER: Badio, Barbara
LEGAL REPRESENTATIVE: Seed and Berry LLP
NUMBER OF CLAIMS: 74
EXEMPLARY CLAIM: 1
LINE COUNT: 5647
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Steroid compounds having various oxygen substitution on the steroid nucleus are disclosed. A specific functionality present on many of the steroid compounds is oxygen substitution at both of positions 6 and 7. Thus, certain steroids have oxygen substitution at C6 and C7, and some have specific stereochemistries such as 6.alpha. and 7.beta. oxygen substitution, and an alpha hydrogen at the 5 position in addition to having 6.alpha. and 7.beta. oxygen substitution. Steroids having 3,4-epoxy functionality are also disclosed. In addition, steroids having C17 pyran and .delta.-lactone functionality, with oxygen substitution at C6 and C7, or at C15, of the steroid nucleus, are disclosed.

IT 809-51-8P
(prepn. of 6,7-oxygenated steroids with therapeutic uses)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 7 OF 75 USPATFULL (Continued)

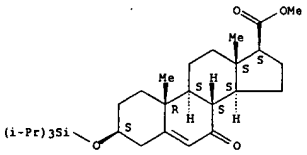


L9 ANSWER 8 OF 75 USPATFULL
ACCESSION NUMBER: 1999:160043 USPATFULL
TITLE: Androstenones
INVENTOR(S): Batchelor, Kenneth William, Durham, NC, United States
Frye, Stephen Vernon, Durham, NC, United States
PATENT ASSIGNEE(S): Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5998427		19991207
APPLICATION INFO.:	US 1998-78468		19980514 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 617859		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kight, John
ASSISTANT EXAMINER: Aulakh, Charanjit S.
LEGAL REPRESENTATIVE: Brink, Robert H.
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 1564
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds of formula (I), wherein carbons 1 and 2 are joined by either a single or a double bond; R.sup.1 is hydrogen or methyl; R.sup.2 is hydrogen or methyl; R.sup.3 is (B) wherein X, R.sup.6, R.sup.7 and R.sup.8 are various groups, and pharmaceutically acceptable solvates thereof and their use in the treatment of androgen responsive and mediated diseases. ##STR1##
IT **164722-13-8P**
(prepn. of azaandrostanones as 5.alpha.-reductase inhibitors)
RN 164722-13-8 USPATFULL
CN Androst-5-ene-17-carboxylic acid, 7-oxo-3-[[tris(1-methylethyl)silyl]oxy]-, methyl ester, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

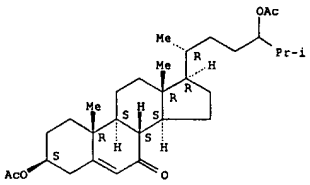


L9 ANSWER 9 OF 75 USPATFULL
ACCESSION NUMBER: 1999:155719 USPATFULL
TITLE: Method of inhibiting proliferation of cells by administering an aminosterol compound
INVENTOR(S): Zasloff, Michael, Merion Station, PA, United States
Shinnar, Ann, Teaneck, NJ, United States
Kinney, William, Churchville, PA, United States
Rao, Meena, Horsham, PA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5994336		19991130
APPLICATION INFO.:	US 1995-479455		19950607 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose' G.
ASSISTANT EXAMINER: Badio, Barbara
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 3505
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of inhibiting the proliferation of a wide variety of cells is described. This method includes administering an effective amount of a compound having the following structure: ##STR1## or a pharmaceutically acceptable salt thereof. The proliferation of the following types of cells can be inhibited by this method: lymphocytes, fibroblasts, epithelial cells, smooth muscle cells, and human ovarian cancer cells.
IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

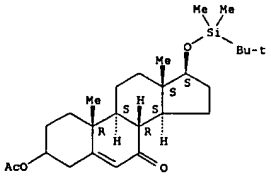


L9 ANSWER 10 OF 75 USPATFULL
ACCESSION NUMBER: 1999:65253 USPATFULL
TITLE: 16-pyrazinyl-substituted-4-aza-androstane 5-.alpha.-reductase isozyme 1 inhibitors
INVENTOR(S): Durette, Philippe L., New Providence, NJ, United States
Hagmann, William K., Westfield, NJ, United States
Lanza, Jr., Thomas J., Edison, NJ, United States
Sahoo, Soumya P., Old Bridge, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Von Langen, Derek, Fanwood, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5910497		19990608
APPLICATION INFO.:	US 1997-991456		19971216 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 601042		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 2582
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the Formula I ##STR1## are inhibitors of the 5.alpha.-reductase 1 isozyme, and are useful alone, or in combination with a 5.alpha.-reductase 2 inhibitor, for the treatment of androgenic sensitive disorders such as acne vulgaris, seborrhea, female hirsutism, male pattern baldness, and benign prostatic hyperplasia.
IT **160496-91-3P**
(prepn. of 16-substituted-4-azaandrostanes as 5.alpha.-reductase isoenzyme 1 inhibitors)
RN 160496-91-3 USPATFULL
CN Androst-5-en-7-one, 3-(acetyloxy)-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

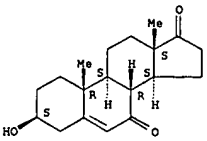


L9 ANSWER 11 OF 75 USPATFULL
ACCESSION NUMBER: 1999:37092 USPATFULL
TITLE: Use of .DELTA.5 androstenes in the treatment of HIV wasting syndrome
INVENTOR(S): Pauza, C. David, Madison, WI, United States
Lardy, Henry A., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, St. Louis Park, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5885977		19990323
APPLICATION INFO.:	US 1997-784856		19970115 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Travers, Russell
LEGAL REPRESENTATIVE: Sherrill, Michael S.
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 577
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB HIV-related weight loss, HIV-related cachexia and HIV-related wasting syndrome can be treated by administering therapeutic amounts of the steroid .DELTA.5-androstene-3.beta.-ol-7,17 dione and metabolizable precursors thereof, such as .DELTA.5-androstene-3.beta.-acetoxy-7,17 dione, which are readily metabolized in vivo to .DELTA.5 androstene-3.beta.-ol-7,17 dione. Such treatment can be prophylactic, modulatory, ameliorative or curative in nature.
IT **566-19-8DP**, precursors **1449-61-2P**
(prepn. and use of .DELTA.5-androstenes in treatment of HIV wasting syndrome)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

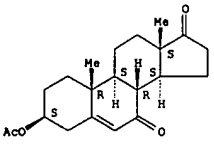
Absolute stereochemistry. Rotation (-).



RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

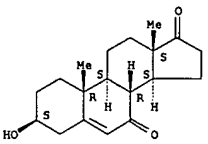
Absolute stereochemistry.

L9 ANSWER 11 OF 75 USPATFULL (Continued)



IT **566-19-8**
(prepn. and use of .DELTA.5-androstenes in treatment of HIV wasting syndrome)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L9 ANSWER 12 OF 75 USPATFULL

ACCESSION NUMBER:	1999:24813 USPATFULL
TITLE:	Certain aminosterol compounds and pharmaceutical compositions including these compounds
INVENTOR(S):	Jones, Steven, West Chester, PA, United States
PATENT ASSIGNEE(S):	Magainin Pharmaceuticals, Inc., Plymouth Meeting, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5874597		19990223
APPLICATION INFO.:	US 1995-476855		19950607 (8)

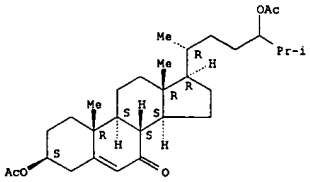
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Prior, Kimberly J.
LEGAL REPRESENTATIVE:	Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS:	5
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	27 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT:	3435

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Aminosterol compounds are described that are useful as inhibitors of the sodium/proton exchanger (NHE). Methods of using such aminosterols compounds are also enclosed, including those employing compounds that are inhibitors of a spectrum of NHEs as well as those using compounds that are inhibitors of only one specific NHE. Advantageous screening techniques and assays for evaluating a compound's therapeutic activity are also disclosed.

IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 13 OF 75 USPATFULL

ACCESSION NUMBER:	1999:22107 USPATFULL
TITLE:	Methods and compositions for treating preterm labor
INVENTOR(S):	Cukierski, Mark A., Souderton, PA, United States Spence, Stanley G., North Wales, PA, United States Waldstreicher, Joanne, Scotch Plains, NJ, United States
PATENT ASSIGNEE(S):	Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5872126		19990216
APPLICATION INFO.:	US 1997-920505		19970829 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-25519P	19960906 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Reamer, James H.
LEGAL REPRESENTATIVE:	Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS:	23
EXEMPLARY CLAIM:	1,19
LINE COUNT:	3830

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

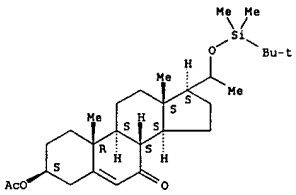
AB The present invention provides for a method of treating preterm labor in a subject in need of such treatment comprising administration of a therapeutically effective amount of an inhibitor of 5.alpha.-reductase type 1 to the subject. The present invention further provides for a method of preventing premature labor in a subject susceptible thereto comprising administration of a labor-preventive amount of an inhibitor of 5.alpha.-reductase type 1 to the subject. Further, the present invention also relates to a method of reducing the risk of premature labor in a subject at risk therefor. The present invention also provides for a method for stopping labor preparatory (i.e., prior) to Cesarean delivery in a subject in need of such treatment comprising administration of a therapeutically effective amount of an inhibitor of 5.alpha.-reductase type 1 to the subject.

Further, the present invention provides for compositions useful in the methods of the present invention, as well as a method of manufacture of a medicament useful for treating pre-term labor and for stopping labor preparatory to Cesarean delivery.

IT **161462-23-3P**
(5.alpha.-reductase inhibitors for treating preterm labor)
RN 161462-23-3 USPATFULL
CN Pregn-5-en-7-one, 3-(acetyloxy)-20-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 13 OF 75 USPATFULL (Continued)

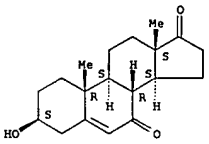


L9 ANSWER 14 OF 75 USPATFULL
ACCESSION NUMBER: 1999:19367 USPATFULL
TITLE: Process for effecting allylic oxidation
INVENTOR(S): Marwah, Padma, Madison, WI, United States
Lardy, Henry A., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, St. Louis Park, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5869709		19990209
APPLICATION INFO.:	US 1997-851939		19970507 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose' G.
ASSISTANT EXAMINER: Pryor, Alton
LEGAL REPRESENTATIVE: Sherrill, Michael S.
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 846
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A procedure for oxidizing organic compounds having allylic hydrogen atom(s) involving the steps of reactively contacting the organic compound with a combination of an alkali metal periodate and an alkyl hydroperoxide. The reaction can conveniently be conducted under ambient temperature and pressure conditions, and is conveniently conducted in a cosolvent system of water and organic solvent(s).
IT **566-19-8P**, 3.beta.-Hydroxyandrost-5-ene-7,17-dione
809-51-8P, 3.beta.-Acetoxy-5-cholesten-7-one **1449-61-2P**
13209-60-4P, 3.beta.,17.beta.-Diacetoxyandrost-5-en-7-one
(allylic oxidn. of allylic compds. using a combination of an alkali metal periodate and an alkyl hydroperoxide)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

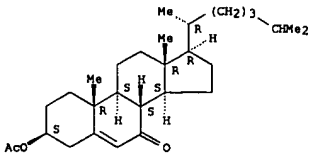
Absolute stereochemistry. Rotation (-).



RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

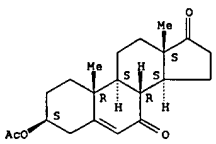
Absolute stereochemistry.

L9 ANSWER 14 OF 75 USPATFULL (Continued)



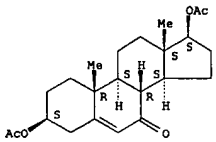
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

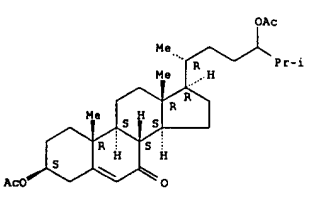


L9 ANSWER 15 OF 75 USPATFULL
ACCESSION NUMBER: 1998:154470 USPATFULL
TITLE: Certain aminosterol compounds and pharmaceutical compositions including these compounds
INVENTOR(S): Zasloff, Michael, Merion Station, PA, United States
Shinnar, Ann, Teaneck, NJ, United States
Kinney, William, Churchville, PA, United States
Jones, Steven, West Chester, PA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5847172		19981208
APPLICATION INFO.:	US 1995-487443		19950607 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Prior, Kimberly J.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 3533
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Aminosterol compounds are described that are useful as inhibitors of the sodium/proton exchanger (NHE). Methods of using such aminosterols compounds are also enclosed, including those employing compounds that are inhibitors of a spectrum of NHEs as well as those using compounds that are inhibitors of only one specific NHE. Advantageous screening techniques and assays for evaluating a compound's therapeutic activity are also disclosed.
IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

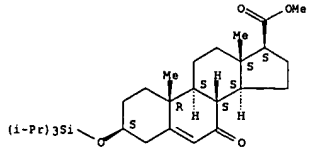


L9 ANSWER 16 OF 75 USPATFULL
ACCESSION NUMBER: 1998:154283 USPATFULL
TITLE: Androstenone derivative
INVENTOR(S): Batchelor, Kenneth William, Chapel Hill, NC, United States
Frye, Stephen Vernon, Durham, NC, United States
Dorsey, Jr., George F., Raleigh, NC, United States
Mook, Jr., Robert A., Chapel Hill, NC, United States
PATENT ASSIGNEE(S): Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5846976		19981208
APPLICATION INFO.:	US 1996-708167		19960822 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-405120, filed on 16 Mar 1995, now patented, Pat. No. US 5565467 which is a continuation-in-part of Ser. No. US 1993-123280, filed on 17 Sep 1993, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fay, Zohreh
LEGAL REPRESENTATIVE: Brink, Robert H.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 782
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the compound of formula (I), ##STR1## also known as 17.beta.-N-(2,5-bis(Trifluoromethyl))phenylcarbamoyl-4-aza-5.alpha.-androst-1-en-3-one, solvates thereof, its preparation, intermediates used in its preparation, pharmaceutical formulations thereof and its use in the treatment of androgen responsive and mediated diseases.
IT **164722-13-8P**
(17.beta.-carbamoyl-4-aza-5.alpha.-androstan-3-ones as selective 5.alpha.-reductase inhibitors)
RN 164722-13-8 USPATFULL
CN Androst-5-ene-17-carboxylic acid, 7-oxo-3-[[tris(1-methylethyl)silyl]oxy]-, methyl ester, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 17 OF 75 USPATFULL

ACCESSION NUMBER: 1998:150955 USPATFULL
TITLE: 7-substituted 4-aza cholanic acid derivatives and their use
INVENTOR(S): Graham, Donald W., Mountainside, NJ, United States
Carlin, Josephine R., Annandale, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Chiu, Shuet-Hing Lee, Westfield, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5843953		19981201	
	WO 9612705		19960502	
APPLICATION INFO.:	US 1997-809506		19970324	(8)
	WO 1995-US13112		19951020	
			19970324	PCT 371 date
			19970324	PCT 102(e) date

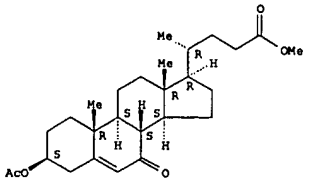
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-328622, filed on 25 Oct 1994, now patented, Pat. No. US 5595996
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rotman, Alan L.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 597
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of formula (I) wherein: the dotted line indicates that a double bond may be present or absent; R.sup.1 is H, methyl or ethyl; R.sup.2 is .alpha.- or .beta.-C.sub.1-10 straight or branched alkyl; R.sup.3 is CO.sub.2 H, CN, CO.sub.2 R.sup.4, COHNR.sup.4, or CON(R.sup.4).sub.2 ; R.sup.4 is H, C.sub.1-10 straight or branched alky, aryl, heteroacyl, or aralkyl; Aryl is phenyl, substituted phenyl, naphthyl, or biphenyl; Heteroaryl is pyridil, pyrrolyl, thienyl, furanyl or quinolinyl; and Aralkyl is C.sub.1-10 alkyl substituted with one to three phenyl or substituted phenyl moieties; and their pharmaceutically acceptable salts are described. These compounds are 5.alpha.-reductase type 1 inhibitors. They may be used for treating conditions associated with an excess of DHT, either alone or in combination with other 5.alpha.-reductase inhibitors. ##STR1##.

IT **121782-71-6**
(synthesis of 4-aza cholanic acid derivs. for use in treatment of conditions assocd. with excess dihydrotestosterone)
RN 121782-71-6 USPATFULL
CN Chol-5-en-24-oic acid, 3-(acetyloxy)-7-oxo-, methyl ester, (3.beta.)- (9CI) (CA INDEX NAME)

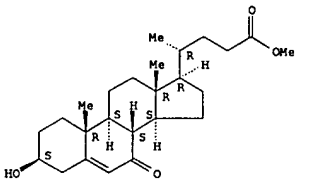
Absolute stereochemistry.

L9 ANSWER 17 OF 75 USPATFULL (Continued)



IT **31427-15-3P 178328-79-5P 178328-80-8P**
(synthesis of 4-aza cholanic acid derivs. for use in treatment of conditions assocd. with excess dihydrotestosterone)
RN 31427-15-3 USPATFULL
CN Chol-5-en-24-oic acid, 3-hydroxy-7-oxo-, methyl ester, (3.beta.)- (9CI) (CA INDEX NAME)

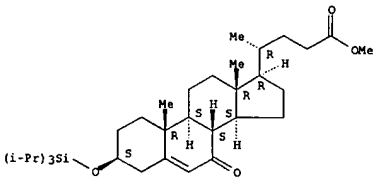
Absolute stereochemistry.



RN 178328-79-5 USPATFULL
CN Chol-5-en-24-oic acid, 7-oxo-3-[[tris(1-methylethyl)silyl]oxy]-, methyl ester, (3.beta.)- (9CI) (CA INDEX NAME)

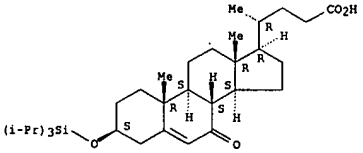
Absolute stereochemistry.

L9 ANSWER 17 OF 75 USPATFULL (Continued)



RN 178328-80-8 USPATFULL
CN Chol-5-en-24-oic acid, 7-oxo-3-[[tris(1-methylethyl)silyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 18 OF 75 USPATFULL

ACCESSION NUMBER: 1998:147645 USPATFULL
TITLE: Aminosterol compounds useful as inhibitors of the sodium/proton exchanger (NHE)
INVENTOR(S): Zasloff, Michael, Merion Station, PA, United States
Shinnar, Ann, Teaneck, NJ, United States
Rao, Meena, Horsham, PA, United States
Kinney, William, Churchville, PA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

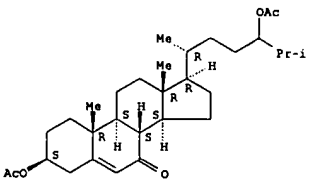
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5840936		19981124	
APPLICATION INFO.:	US 1995-475572		19950607	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Geist, Gary
ASSISTANT EXAMINER: Frazier, Barbara S.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 3497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Aminosterol compounds are described that are useful as inhibitors of the sodium/proton exchanger (NHE). Methods of using such aminosterols compounds are also enclosed, including those employing compounds that are inhibitors of a spectrum of NHEs as well as those using compounds that are inhibitors of only one specific NHE. Advantageous screening techniques and assays for evaluating a compound's therapeutic activity are also disclosed.

IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

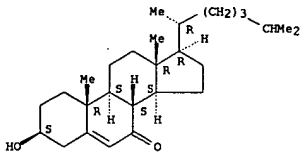


L9 ANSWER 19 OF 75 USPATFULL
ACCESSION NUMBER: 1998:147467 USPATFULL
TITLE: Reduction of hair growth
INVENTOR(S): Henry, James P., 10257 Meadow Fence Ct., Myersville, MD, United States 21773
Ahluwalia, Gurpreet S., 8632 Stableview Ct., Gaithersburg, MD, United States 20882
Shander, Douglas, 16112 Howard Landing Dr., Gaithersburg, MD, United States 20878

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5840752		19981124
APPLICATION INFO.:	US 1996-754556		19961121 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: MacMillan, Keith D.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
LINE COUNT: 328
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mammalian hair growth is reduced by applying to the skin an inhibitor of a cholesterol synthetic pathway enzyme.
IT **566-28-9**, 7-Ketocholesterol
(skin application of inhibitors of cholesterol synthetic pathway enzymes for redn. of unwanted hair growth)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

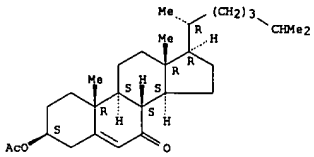


L9 ANSWER 20 OF 75 USPATFULL
ACCESSION NUMBER: 1998:147455 USPATFULL
TITLE: Aminosterol compounds and a method of treating infection using the aminosterol compounds
INVENTOR(S): Zasloff, Michael, Merion Station, PA, United States
Shinnar, Ann, Teaneck, NJ, United States
Kinney, William, Churchville, PA, United States
Rao, Meena, Horsham, PA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5840740		19981124
APPLICATION INFO.:	US 1995-483059		19950607 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose G.
ASSISTANT EXAMINER: Badio, Barbara
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 3513
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are aminosterol compounds 1360 and 1361: ##STR1## which can be obtained in isolated or purified form from the liver of the dogfish shark.
IT **809-51-8P 166896-76-0P**
(isolation, prepn., and Na+-H+ exchanger-inhibiting activity of aminosterols)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

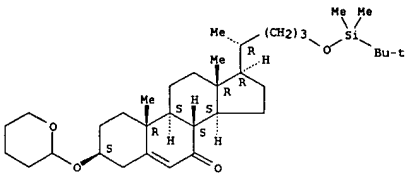
Absolute stereochemistry.



RN 166896-76-0 USPATFULL
CN Chol-5-en-7-one, 24-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(tetrahydro-2H-pyran-2-yl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 20 OF 75 USPATFULL (Continued)



L9 ANSWER 21 OF 75 USPATFULL
ACCESSION NUMBER: 1998:143677 USPATFULL
TITLE: Vaccine compositions and method for enhancing an immune response
INVENTOR(S): Daynes, Raymond A., Park City, UT, United States
Araneo, Barbara A., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): University of Utah Research Foundation, Salt Lake City, UT, United States (U.S. corporation)

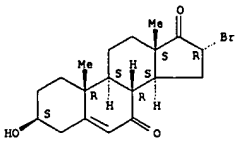
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5837269		19981117
APPLICATION INFO.:	US 1995-487173		19950607 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-123843, filed on 9 Sep 1993, now patented, Pat. No. US 5562910 which is a continuation-in-part of Ser. No. US 1993-13972, filed on 4 Feb 1993, now abandoned And Ser. No. US 1991-779499, filed on 18 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-412270, filed on 25 Sep 1989, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Caputa, Anthony C.
ASSISTANT EXAMINER: Masood, Khalid
LEGAL REPRESENTATIVE: Rothwell, Figg, Ernst & Kurz, P.C.
NUMBER OF CLAIMS: 50
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 46 Drawing Figure(s); 18 Drawing Page(s)
LINE COUNT: 2026
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a vaccine which comprises an antigen and an immune response augmenting agent. The immune response augmenting agent is capable of enhancing T cell lymphokine production. Suitable immune response augmenting agents include, but are not limited to, DHEA, DHEA-derivatives and DHEA congeners.

The invention also relates to a method for enhancing a vaccine-induced humoral immune response which comprises administering a vaccine which comprises an antigen and an immunomodulator. The immunomodulator may be an immune response augmenting agent, a lymphoid organ modifying agent or a mixture of the immune response augmenting agent and lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include, but are not limited to, 1,25-dihydroxy Vitamin D.sub.3, 25-hydroxy Vitamin D.sub.3, biologically active 1,25-dihydroxy Vitamin D.sub.3, derivatives which are capable of activating the intra-cellular Vitamin D.sub.3 receptor, all trans-retinoic acid, retinoic acid derivatives, retinol, retinol derivatives and glucocorticoid. Alternatively, the method for enhancing a vaccine-induced humoral immune response comprises separately administering the immunomodulator and a vaccine containing an antigen.
IT **216062-79-2 216062-88-3 216062-89-4 216062-99-6 216063-03-5**
(vaccine compns. and method for enhancing an immune response)
RN 216062-79-2 USPATFULL
CN Androst-5-ene-7,17-dione, 16-bromo-3-hydroxy-, (3.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

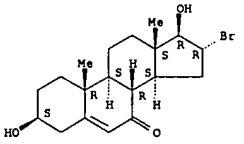
Absolute stereochemistry.

L9 ANSWER 21 OF 75 USPATFULL (Continued)



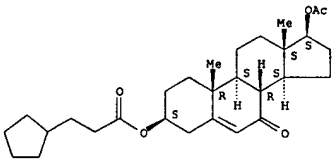
RN 216062-88-3 USPATFULL
CN Androst-5-en-7-one, 16-bromo-3,17-dihydroxy-, (3.beta.,16.alpha.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 216062-89-4 USPATFULL
CN Androst-5-en-7-one, 17-(acetyloxy)-3-(3-cyclopentyl-1-oxopropoxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

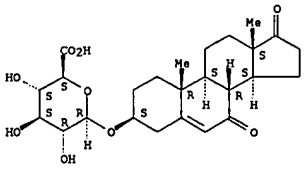
Absolute stereochemistry.



RN 216062-99-6 USPATFULL
CN .beta.-D-Glucopyranosiduronic acid, (3.beta.)-7,17-dioxoandrost-5-en-3-yl (9CI) (CA INDEX NAME)

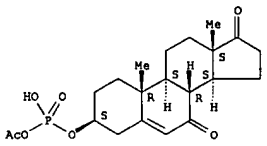
Absolute stereochemistry.

L9 ANSWER 21 OF 75 USPATFULL (Continued)



RN 216063-03-5 USPATFULL
CN Androst-5-ene-7,17-dione, 3-[[(acetyloxy)hydroxyphosphinyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 22 OF 75 USPATFULL

ACCESSION NUMBER:	1998:122564 USPATFULL
TITLE:	Androstenones
INVENTOR(S):	Batchelor, Kenneth William, Durham, NC, United States Frye, Stephen Vernon, Durham, NC, United States
PATENT ASSIGNEE(S):	Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5817818		19981006	
	WO 9507926		19950323	
APPLICATION INFO.:	US 1996-617859		19960314	(8)
	WO 1994-US10479		19940916	
			19960314	PCT 371 date
			19960314	PCT 102(e) date

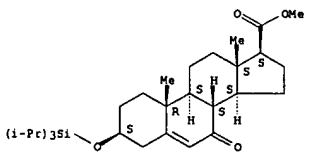
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Brink, Robert H.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 1606
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to compounds of formula (I), wherein carbons 1 and 2 are joined by either a single or a double bond; R.sup.1 is hydrogen or methyl; R.sup.2 is hydrogen or methyl; R.sup.3 is (A) or (B) wherein X, W, Z, R.sup.4, R.sup.5, R.sup.6, R.sup.7 and R.sup.8 are various groups, and pharmaceutically acceptable solvates thereof and their use in the treatment of androgen responsive and mediated diseases. ##STR1##

IT **164722-13-8P**
(17.beta.-carbamoyl-4-aza-5.alpha.-androstan-3-ones as selective 5.alpha.-reductase inhibitors)

RN 164722-13-8 USPATFULL
CN Androst-5-ene-17-carboxylic acid, 7-oxo-3-[[tris(1-methylethyl)silyl]oxy]-, methyl ester, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 23 OF 75 USPATFULL

ACCESSION NUMBER:	1998:122548 USPATFULL
TITLE:	Process for the stereoselective reduction of steroid enelactams
INVENTOR(S):	Humphrey, Guy R., Belle Mead, NJ, United States Miller, Ross A., Fanwood, NJ, United States
PATENT ASSIGNEE(S):	Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5817802		19981006	
APPLICATION INFO.:	US 1997-776735		19970205	(8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-508804, filed on 28 Jul 1995, now patented, Pat. No. US 5696266 which is a continuation-in-part of Ser. No. US 1994-301949, filed on 7 Sep 1994, now patented, Pat. No. US 5470976			

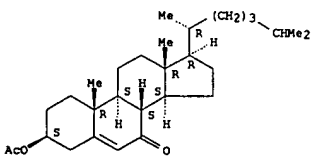
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Raymond, Richard L.
ASSISTANT EXAMINER: Rao, Deepak R.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 1225
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The novel process of this invention involves the reduction of certain .DELTA.-5 steroidal alkenes to selectively produce either the 5.alpha. or 5.beta. reduction products. Particularly, this invention involves reduction of .DELTA.-5 steroidal alkenes using a rhodium based catalyst in the presence of hydrogen to selectively yield 5.alpha. steroids or alternatively reduction of .DELTA.-5 steroidal alkenes in an ionizing medium with a trialkylsilane to selectively yield 5.beta. steroids.

IT **809-51-8P**, 7-Oxocholesteryl acetate
(stereoselective redn. of azacholestenones)

RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 24 OF 75 USPATFULL

ACCESSION NUMBER: 1998:98909 USPATFULL
TITLE: Method of inhibiting profileration of cells by administering an aminosterol compound
INVENTOR(S): Zasloff, Michael, Merion Station, PA, United States
Shinnar, Ann, Teaneck, NJ, United States
Kinney, William, Churchville, PA, United States
Anderson, Mark, Norristown, PA, United States
Williams, Jon, Robbinsville, NJ, United States
McLane, Michael, Lansdale, PA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

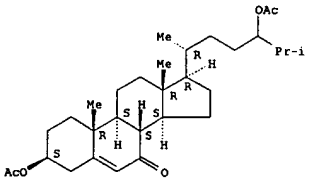
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5795885		19980818
APPLICATION INFO.:	US 1995-483057		19950607 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rollins, John W.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 3513
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Aminosterol compounds are described that are useful as inhibitors of the sodium/proton exchanger (NHE). Methods of using such aminosterols compounds are also disclosed, including those employing compounds that are inhibitors of a spectrum of NHEs as well as those using compounds that are inhibitors of only one specific NHE. Advantageous screening techniques and assays for evaluating a compound's therapeutic activity are also disclosed.

IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 24 OF 75 USPATFULL (Continued)

L9 ANSWER 25 OF 75 USPATFULL

ACCESSION NUMBER: 1998:95412 USPATFULL
TITLE: Method of inhibiting the sodium/proton exchanger NHE3 and method of inhibiting growth by administering squalamine
INVENTOR(S): Zasloff, Michael, Merion Station, PA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals, Inc., Plymouth Meeting, PA, United States (U.S. corporation)

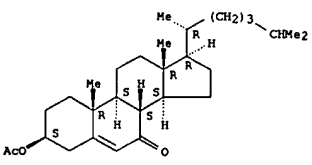
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5792635		19980811
APPLICATION INFO.:	US 1995-474799		19950607 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gitomer, Ralph
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 3485
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Aminosterol compounds are described that are useful as inhibitors of the sodium/proton exchanger (NHE). Methods of using such aminosterols compounds are also disclosed, including those employing compounds that are inhibitors of a spectrum of NHEs as well as those using compounds that are inhibitors of only one specific NHE. Advantageous screening techniques and assays for evaluating a compound's therapeutic activity are also disclosed.

IT **809-51-8P 166896-76-0P**
(use of squalamine for the manuf. of a medicament for inhibiting the sodium-proton exchanger)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

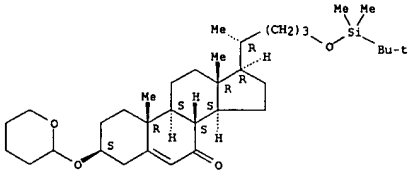
Absolute stereochemistry.



RN 166896-76-0 USPATFULL
CN Chol-5-en-7-one, 24-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(tetrahydro-2H-pyran-2-yl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 25 OF 75 USPATFULL (Continued)



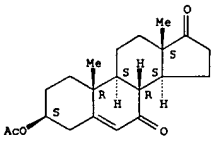
L9 ANSWER 26 OF 75 USPATFULL
ACCESSION NUMBER: 1998:65216 USPATFULL
TITLE: Pharmaceutical compositions containing 3-beta-hydroxylated 6,7-substituted steroid derivatives, and use thereof
INVENTOR(S): Morfin, Robert, Paris, France
PATENT ASSIGNEE(S): Conservatoire National des Arts et Metiers, Paris, France (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5763433		19980609	
	WO 9408588		19940428	
APPLICATION INFO.:	US 1995-416868		19950621	(8)
	WO 1993-FR1029		19931019	
			19950621	PCT 371 date
			19950621	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	FR 1992-12548	19921020

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Nixon & Vanderhye P.C.
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 905
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical composition containing 7-hydroxylated derivatives of natural steroid hormones having, if necessary, a 3.beta. hydroxyl function, for use as an immunity trigger or stimulant (hereinafter termed "immunity effector"), particularly for cell immunity. Said pharmaceutical compositions may also be used as anti-glucocorticoid agents.
IT **1449-61-2P**, 3.beta.-Acetoxy-androst-5-ene-7,17-dione
(prepn. and redn. of)
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



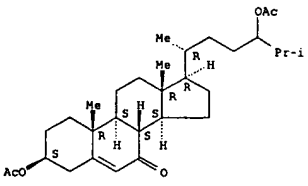
L9 ANSWER 26 OF 75 USPATFULL (Continued)

L9 ANSWER 27 OF 75 USPATFULL
ACCESSION NUMBER: 1998:65213 USPATFULL
TITLE: Method of treating a viral infection by administering a steroid compound
INVENTOR(S): Zasloff, Michael, Merion Station, PA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5763430		19980609	
APPLICATION INFO.:	US 1995-479457		19950607	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Prior, Kimberly J.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 20 Drawing Page(s)
LINE COUNT: 3495
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of treating a viral infection includes administering an effective amount of a compound having the following structure: ##STR1## or a pharmaceutically acceptable salt thereof. This compound treats the viral infection by suppressing the growth of a viral target cell. As one specific example, this compound may be used to treat HIV infection.
IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 28 OF 75 USPATFULL
ACCESSION NUMBER: 1998:65148 USPATFULL
TITLE: 17-alkyl-7-substituted-4-aza steroid derivatives as 5-.alpha.-reductase inhibitors
INVENTOR(S): Harris, Georgianna, Tinton Falls, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Sahoo, Soumya P., Old Bridge, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

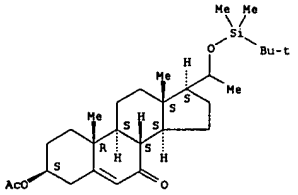
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5763361		19980609	
APPLICATION INFO.:	US 1996-734705		19961021	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1995-5832P	19951023 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 1269
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The novel compounds of the present invention are those of structural formula I: ##STR1## or a pharmaceutically acceptable salt, or stereoisomer thereof, which are inhibitors of 5.alpha.-reductase, particularly 5.alpha.-reductase type 1. The compounds of formula I are useful in the systemic, including oral, or parenteral or topical treatment of hyperandrogenic conditions such as acne vulgaris, seborrhea, androgenic alopecia which includes female and male pattern baldness, female hirsutism, benign prostafic hyperplasia, and the prevention and treatment of prostatic carcinoma, as well as in the treatment of prostatitis. Methods of using the compounds of formula I for the treatment of hyperandrogenic conditions such as acne vulgaris, seborrhea, androgenic alopecia, male pattern baldness, female hirsutism, benign prostatic hyperplasia, and the prevention and treatment of prostatic carcinoma, as well as the treatment of prostatitis are provided, as well as pharmaceutical compositions for the compounds of formula I. The use of compounds of formula I in combination with other, active agents, for example with a 5.alpha.-reductase type 2 inhibitor such as finasteride or epristeride, or a potassium channel opener, such as minoxidil, or a retinoic acid or a derivative thereof is also taught, wherein such combinations would be useful in one or more of the above-mentioned methods of treatment or pharmaceutical compositions.
IT **161462-23-3P**, 3-Acetoxy-20-[(tert-butyldimethylsilyl)oxy]pregn-5-en-7-one
(prepn. of 17-alkyl-7-substituted-4-aza steroid derivs. as 5-.alpha.-reductase inhibitors)
RN 161462-23-3 USPATFULL
CN Pregn-5-en-7-one, 3-(acetyloxy)-20-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 28 OF 75 USPATFULL (Continued)



L9 ANSWER 29 OF 75 USPATFULL

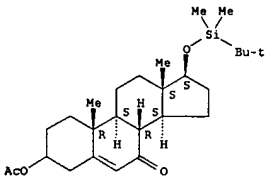
ACCESSION NUMBER: 1998:39528 USPATFULL
TITLE: 16-substituted-4-aza-3-oxo-androstane as 5-alpha-reductase isozyme 1 inhibitors
INVENTOR(S): Durette, Philippe L., New Providence, NJ, United States
Hagmann, William K., Westfield, NJ, United States
Lanza, Jr., Thomas J., Edison, NJ, United States
Sahoo, Soumya P., Old Bridge, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Von Langen, Derek, Fanwood, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5739137		19980414	
	WO 9511254		19950427	
APPLICATION INFO.:	US 1996-601042		19960228	(8)
	WO 1994-US12071		19941021	
			19960228	PCT 371 date
			19960228	PCT 102(e) date

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-141153, filed on 21 Oct 1993, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Nicholson, William H., Winokur, Melvin
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 2621
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (I) are inhibitors of the 5.alpha.-reductase 1 isozyme, and are useful alone, or in combination with a 5.alpha.-reductase 2 inhibitor, for the treatment of androgenic sensitive disorders such as acne vulgaris, seborrhea, female hirsutism, male pattern baldness, and benign prostatic hyperplasia. ##STR1##
IT **160496-91-3P**
(prepn. of 16-substituted-4-aza-3-oxoandrostanes as 5.alpha.-reductase isoenzyme 1 inhibitors)
RN 160496-91-3 USPATFULL
CN Androst-5-en-7-one, 3-(acetyloxy)-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 29 OF 75 USPATFULL (Continued)



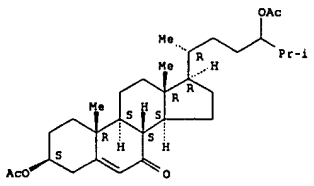
L9 ANSWER 30 OF 75 USPATFULL

ACCESSION NUMBER: 1998:33921 USPATFULL
TITLE: Method for treating infection using steroid based pharmaceutical compositions
INVENTOR(S): Frye, Leah L., Ravena, NY, United States
Zasloff, Michael A., Merion Station, PA, United States
Kinney, William A., Churchill, PA, United States
Moriarty, Robert, Oak Park, IL, United States
Collins, Delwood C., Lexington, KY, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5733899		19980331	
	WO 9524415		19950914	
APPLICATION INFO.:	US 1995-416883		19950420	(8)
	WO 1994-US10265		19940913	
			19950420	PCT 371 date
			19950420	PCT 102(e) date

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-29018, filed on 10 Mar 1993, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose G.
ASSISTANT EXAMINER: Badio, Barbara
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 1620
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of treating a bacterial or fungal infection in a patient by administering an effective amount of a compound of Formula (III): ##STR1## wherein, the substituents are as defined in the specification.
IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

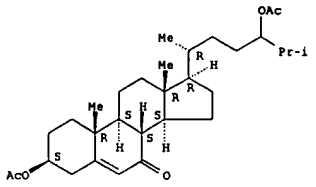


L9 ANSWER 31 OF 75 USPATFULL
ACCESSION NUMBER: 1998:19695 USPATFULL
TITLE: Method for inhibiting angiogenesis using squalamine and squalamine steroid derivatives
INVENTOR(S): Frye, Leah L., Ravena, NY, United States
Zasloff, Michael A., Merion Station, PA, United States
Kinney, William A., Churchill, PA, United States
Moriarty, Robert, Oak Park, IL, United States
Collins, Delwood C., Lexington, KY, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5721226		19980224
APPLICATION INFO.:	US 1995-478763		19950607 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-416883, filed on 20 Apr 1995 And a continuation-in-part of Ser. No. US 1994-290826, filed on 18 Aug 1994, now patented, Pat. No. US 5637691 And a continuation-in-part of Ser. No. US 1993-29018, filed on 10 Mar 1993, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Prior, Kimberly J.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett, & Dunner, L.L.P.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 1659
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of inhibiting angiogenesis in a patient includes administering to the patient an effective amount of squalamine or a pharmaceutically acceptable salt of squalamine. Alternatively, a compound according to the following Formula (III) (or a pharmaceutically acceptable salt thereof) can be administered: ##STR1## wherein Z.sub.5 is .alpha.-H or .beta.-H; each of the substituents Z.sub.7 is selected from the group of --H, --OH, --SH, --NH.sub.2, --F, --(C.sub.1 -C.sub.3)-alkyl, and --(C.sub.1 -C.sub.3)-alkoxy; and one of the substituents Z.sub.12 is --H and the other is --H or --OH. X' is a polyamine side chain of the formula --X.sub.1 --(CH.sub.2).sub.p --X.sub.2 --(CH.sub.2).sub.q --N(R.sup.II)(R.sup.III), wherein one of X.sub.1 and X.sub.2 is --N(R.sup.IV) and the other is selected from the group of --N(R.sup.V), --O, --S, and --CH.sub.2. R.sup.IV and R.sup.V are each --H or --(C.sub.1 -C.sub.3)-alkyl, p and q are each an integer of from 0 to 5 (but both are not 0). R.sup.II and R.sup.III in the formula for X' are each --H, --(C.sub.1 -C.sub.3)-alkyl, or --(CH.sub.2).sub.r --N(R.sub.10)(R.sub.11) wherein r is an integer from 2 to 5 and R.sub.10 and R.sub.11 are each --H or --(C.sub.1 -C.sub.3)-alkyl. R' in Formula (III) is --H or --(C.sub.1 -C.sub.3)-alkyl, and Y' is --(C.sub.1 -C.sub.10)-alkyl, unsubstituted or substituted with --CO.sub.2 H, --OH, --NH--SO.sub.2 CF.sub.3, --SO.sub.3 H, --PO.sub.3 H.sub.2, --OSO.sub.3 H, --CF.sub.3, --F, ##STR2##
IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

L9 ANSWER 31 OF 75 USPATFULL (Continued)
Absolute stereochemistry.

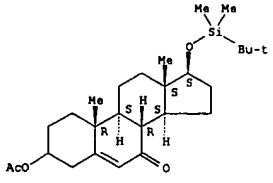


L9 ANSWER 32 OF 75 USPATFULL
ACCESSION NUMBER: 1998:17321 USPATFULL
TITLE: 16-substituted-4-aza-androstane 5-alpha-reductase isozyme 1 inhibitors
INVENTOR(S): Durette, Philippe L., New Providence, NJ, United States
Hagmann, William K., Westfield, NJ, United States
Lanza, Jr., Thomas J., Edison, NJ, United States
Sahoo, Soumya P., Old Bridge, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
Tolman, Richard L., Warren, NJ, United States
von Langen, Derek, Fanwood, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5719158		19980217
APPLICATION INFO.:	US 1995-463544		19950605 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-141153, filed on 21 Oct 1993, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
LINE COUNT: 2932
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the Formula I ##STR1## are inhibitors of the 5.alpha.-reductase 1 isozyme, and are useful alone, or in combination with a 5.alpha.-reductase 2 inhibitor, for the treatment of androgenic sensitive disorders such as acne vulgaris, seborrhea, female hirsutism, male pattern baldness, and benign prostatic hyperplasia.
IT **160496-91-3P**
(prepn. of 16-substituted-4-azaandrostanes as 5.alpha.-reductase isoenzyme 1 inhibitors)
RN 160496-91-3 USPATFULL
CN Androst-5-en-7-one, 3-(acetyloxy)-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

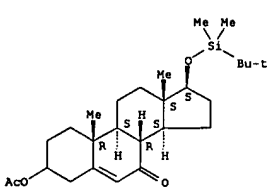


L9 ANSWER 33 OF 75 USPATFULL
ACCESSION NUMBER: 1998:7190 USPATFULL
TITLE: 7.beta.-substituted-4-aza-5.alpha.-androstan-3-ones as 5.alpha.-reductase inhibitors
INVENTOR(S): Bakshi, Raman K., Edison, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Patel, Gool F., Califon, NJ, United States
Harris, Georgianna S., Tinton Falls, NJ, United States
Graham, Donald W., Mountainside, NJ, United States
Witzel, Bruce E., Westfield, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5710275		19980120	
	WO 9323420		19931125	
APPLICATION INFO.:	US 1995-341602		19950403	(8)
	WO 1993-US4643		19930514	
			19950403	PCT 371 date
			19950403	PCT 102(e) date

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-886572, filed on 20 May 1992, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Nicholson, William H., Winokur, Melvin
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 5206
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Described are new 7.beta.-substituted 4-aza-5.alpha.-androstan-3-ones and related compounds as 5.alpha.-reductase inhibitors.
IT **160496-91-3P**
(prepn. of azaandrostanones as 5.alpha.-reductase inhibitors)
RN 160496-91-3 USPATFULL
CN Androst-5-en-7-one, 3-(acetyloxy)-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 34 OF 75 USPATFULL
ACCESSION NUMBER: 1998:4582 USPATFULL
TITLE: Treatment of alzheimer's disease and modulation of immune system with .DELTA.5-androstenes
INVENTOR(S): Lardy, Henry A., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, St. Louis Park, MN, United States (U.S. corporation)

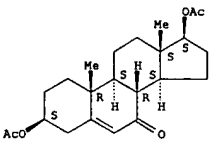
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5707983		19980113
APPLICATION INFO.:	US 1997-806541		19970224 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-527746, filed on 13 Sep 1995, now patented, Pat. No. US 5641766 which is a continuation-in-part of Ser. No. US 1992-867288, filed on 10 Apr 1992, now patented, Pat. No. US 5296481 which is a continuation of Ser. No. US 1990-575156, filed on 29 Aug 1990, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Sherrill, Michael S.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 499
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Alzheimer's disease and immune deficiency disorders may be effectively treated by administering a .DELTA.5-Androstene-3.beta.-ol-17-one having a C.sub.7 substituent selected from the group consisting of oxo, hydroxy and groups convertible thereto by hydrolysis by administering a therapeutic amount of a .DELTA.5-Androstene-3.beta.-ol-17-one having a C.sub.7 substituent selected from the group consisting of oxo, hydroxy and groups convertible thereto by hydrolysis.

IT **13209-60-4**
(glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)
RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

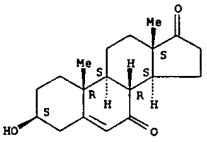
Absolute stereochemistry.



IT **1449-61-2P**
(prepn. of and glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)

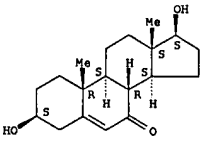
L9 ANSWER 34 OF 75 USPATFULL (Continued)
(wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



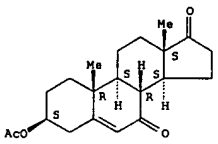
RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



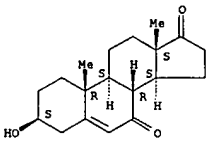
L9 ANSWER 34 OF 75 USPATFULL (Continued)
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



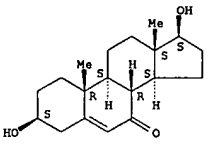
IT **566-19-8P 2226-65-5P**
(prepn. of and wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **566-19-8D, esters 2226-65-5D, esters**

L9 ANSWER 35 OF 75 USPATFULL
ACCESSION NUMBER: 97:115422 USPATFULL
TITLE: Process for the stereoselective reduction of steroid enelactams
INVENTOR(S): Humphrey, Guy R., Belle Mead, NJ, United States
Miller, Ross A., Fanwood, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

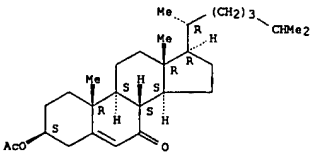
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5696266		19971209
APPLICATION INFO.:	US 1995-508804		19950728 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-301949, filed on 7 Sep 1994, now patented, Pat. No. US 5470976
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 1197
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The novel process of this invention involves the reduction of certain .DELTA.-5 steroidal alkenes to selectively produce either the 5.alpha. or 5.beta. reduction products. Particularly, this invention involves reduction of .DELTA.-5 steroidal alkenes using a rhodium based catalyst in the presence of hydrogen to selectively yield 5.alpha. steroids or alternatively reduction of .DELTA.-5 steroidal alkenes in an ionizing medium with a trialkylsilane to selectively yield 5.beta. steroids.

IT **809-51-8P**
(stereoselective redn. of steroid enelactams)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

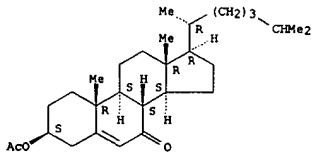


L9 ANSWER 36 OF 75 USPATFULL
ACCESSION NUMBER: 97:112633 USPATFULL
TITLE: Substituted 4-aza-5.alpha.-androstan-ones as 5.alpha.-reductase inhibitors
INVENTOR(S): Durette, Philippe L., New Providence, NJ, United States
Hagmann, William, Westfield, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Kopka, Ihor E., Millburn, NJ, United States
Sahoo, Soumya P., Old Bridge, NJ, United States
Esser, Craig K., Belford, NJ, United States
Steinberg, Nathan G., Clark, NJ, United States
Graham, Donald W., Mountainside, NJ, United States
Witzel, Bruce E., Westfield, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5693809		19971202
APPLICATION INFO.:	US 1995-338571		19950512 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1992-886537, filed on 20 May 1992, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
LINE COUNT: 8954
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Described are new 16-substituted and 7,16-disubstituted 4-aza-5.alpha.-androstan-3-ones and related compounds as 5.alpha.-reductase inhibitors.
IT **809-51-8**
(prepn. of substituted 4-aza-3-oxo-5.alpha.-steroids for use as 5.alpha.-reductase inhibitors)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



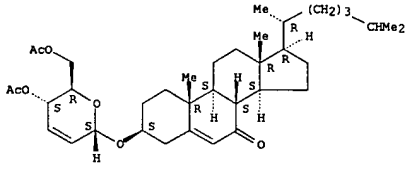
L9 ANSWER 37 OF 75 USPATFULL
ACCESSION NUMBER: 97:112593 USPATFULL
TITLE: Glycoside derivatives of acetaminophen
INVENTOR(S): Klemke, R. -Erich, Hilzingen, Germany, Federal Republic of
Koreeda, Masato, Ann Arbor, MI, United States
Houston, Todd A., Timonium, MD, United States
Shull, Brian K., Ann Arbor, MI, United States
Tuinman, Roeland J., Fenton, MI, United States
PATENT ASSIGNEE(S): Harrier Inc., Hermosa Beach, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5693767		19971202
APPLICATION INFO.:	US 1994-251869		19940601 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-6447, filed on 21 Jan 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-815691, filed on 24 Jan 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-733915, filed on 22 Jul 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-644002, filed on 22 Jan 1991, now patented, Pat. No. US 5278296, issued on 11 Jan 1994		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kight, John
ASSISTANT EXAMINER: Lee, Howard C.
LEGAL REPRESENTATIVE: Medlen & Carroll, LLP
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1043
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel glycosides, especially steroidal and non-steroidal glycosides are provided. The steroidal and non-steroidal glycosides preferably are prepared from aglycons which possess valuable properties such as pharmacological properties. The glycosides are prepared from useful aglycons and possess useful properties which are the same as those of their respective unglycosylated aglycons. The glycosides are provided in acylated and deacylated form. The acylated glycosides after hydrolysis of the acyl groups possess enhanced water solubility properties, as illustrated in the case where the aglycon is acetominophen.
IT **136468-12-7P**
(prepn. and water soly. acetaminophen glycosides)
RN 136468-12-7 USPATFULL
CN Cholest-5-en-7-one, 3-[(4,6-di-O-acetyl-2,3-dideoxy-.alpha.-D-erythro-hex-2-enopyranosyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 37 OF 75 USPATFULL (Continued)

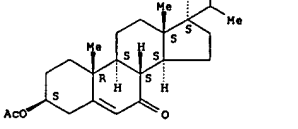


L9 ANSWER 38 OF 75 USPATFULL
ACCESSION NUMBER: 97:73629 USPATFULL
TITLE: 4-aza-pregnane 5.alpha.-reductase isozyme 1 inhibitors
INVENTOR(S): Durette, Philippe L., New Providence, NJ, United States
Sahoo, Soumya P., Old Bridge, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5658922		19970819
	WO 9500147		19950105
APPLICATION INFO.:	US 1995-537876		19951031 (8)
	WO 1994-US7220		19940627
			19951031 PCT 371 date
			19951031 PCT 102(e) date
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-83798, filed on 28 Jun 1993, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
LINE COUNT: 851
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (I), wherein: R.sup.1 is selected from the group consisting of hydrogen and methyl; R.sup.2 is selected from the group consisting of methyl and ethyl; R.sup.3 is selected from the group consisting of hydrogen and methyl; and the C1-C2 carbon-carbon bond may be a single or double bond. Such compounds are useful in the treatment of pathologic conditions that benefit from blockade of isozymes of 5.alpha.-reductase. ##STR1##
IT **161462-23-3P**
(prepn. of azapregnanes as 5.alpha.-reductase isoenzyme 1 inhibitors)
RN 161462-23-3 USPATFULL
CN Pregn-5-en-7-one, 3-(acetyloxy)-20-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

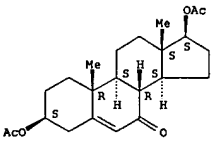


L9 ANSWER 39 OF 75 USPATFULL
ACCESSION NUMBER: 97:54216 USPATFULL
TITLE: UP-regulation of immune system with .DELTA.5-Androstenes
INVENTOR(S): Lardy, Henry A., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, St. Louis Park, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5641766		19970624
APPLICATION INFO.:	US 1995-527746		19950913 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1993-132802, filed on 7 Oct 1993, now abandoned which is a division of Ser. No. US 1992-922850, filed on 31 Jul 1992, now patented, Pat. No. US 5292730 which is a continuation-in-part of Ser. No. US 1992-867288, filed on 10 Apr 1992, now patented, Pat. No. US 5296481 which is a continuation of Ser. No. US 1990-575156, filed on 29 Aug 1990, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Sherrill, Michael S.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 477
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Alzheimer's disease and immune deficiency disorders may be effectively treated by administering a .DELTA.5-Androstene-3.beta.-ol-17-one having a C.sub.7 substituent selected from the group consisting of oxo, hydroxy and groups convertible thereto by hydrolysis by administering a therapeutic amount of a .DELTA.5-Androstene-3.beta.-ol-17-one having a C.sub.7 substituent selected from the group consisting of oxo, hydroxy and groups convertible thereto by hydrolysis.
IT **13209-60-4**
(glycerol 3-phosphate dehydrogenase and malic enzyme induction response to, in rat liver)
RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

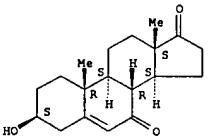
Absolute stereochemistry.



IT **1449-61-2P**
(prepn. of and glycerol 3-phosphate dehydrogenase and malic enzyme

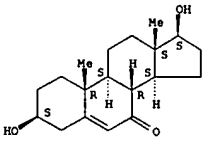
L9 ANSWER 39 OF 75 USPATFULL (Continued)
IT **566-19-8D**, esters **2226-65-5D**, esters
(wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



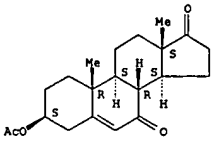
RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



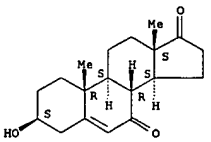
L9 ANSWER 39 OF 75 USPATFULL (Continued)
induction response to, in rat liver)
RN 1449-61-2 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



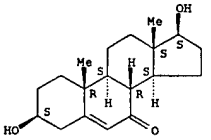
IT **566-19-8P 2226-65-5P**
(prepn. of and wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



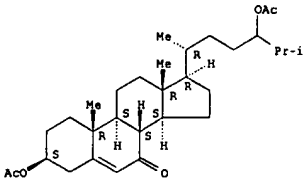
L9 ANSWER 40 OF 75 USPATFULL
ACCESSION NUMBER: 97:49738 USPATFULL
TITLE: Steroid derivatives, pharmaceutical compositions containing them, and their use as antibiotics or disinfectants
INVENTOR(S): Frye, Leah L., Ravena, NY, United States
Zasloff, Michael A., Merion Station, PA, United States
Kinney, William A., Churchville, PA, United States
Moriarty, Robert, Oak Park, IL, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals, Inc., Plymouth Meeting, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5637691		19970610	
	WO 9420520		19940915	
APPLICATION INFO.:	US 1994-290826		19940818	(8)
	WO 1994-US2397		19940316	
			19940818	PCT 371 date
			19940818	PCT 102(e) date
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-29018, filed on 10 Mar 1993, now abandoned			

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Cook, Rebecca
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 1576
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds having a broad range of antimicrobial activity generally have a structure including asteroid nucleus with a cationic, preferably polyamine, side chain (X) and an anionic side chain (Y). The invention is also directed to compounds of the Formula III: ##STR1## preferably where the steroid ring nucleus is saturated; the steroid ring substituent Z.sub.5 is .alpha.-H; one Z.sub.7 is .beta.-H and the other is .alpha.-H or .alpha.-OH; both substituents Z.sub.12 are hydrogen; X' is a polyamine side chain of the formula --NH--(CH.sub.2).sub.p --NH--(CH.sub.2).sub.q --N(R.sup.II)(R.sup.III) where p and q are each independently 3 or 4, and R.sup.II and R.sup.III are each independently hydrogen or methyl; R' is methyl; and Y' is (C.sub.1 -C.sub.10)-alkyl substituted with a group such as --CO.sub.2 H or --SO.sub.3 H.
IT **160348-83-4P**
(prepn. of polyaminosteroids as bactericides and antifungals)
RN 160348-83-4 USPATFULL
CN Cholest-5-en-7-one, 3,24-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 40 OF 75 USPATFULL (Continued)



L9 ANSWER 41 OF 75 USPATFULL

ACCESSION NUMBER: 97:5975 USPATFULL
TITLE: 7-substituted 4-aza cholanic acid derivatives and their use
INVENTOR(S): Graham, Donald W., Mountainside, NJ, United States
Carlin, Josephine R., New Brunswick, NJ, United States
Chiu, Shuet-Hing L., Westfield, NJ, United States
Tolman, Richard L., Warren, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5595996		19970121
APPLICATION INFO.:	US 1994-328622		19941025 (8)

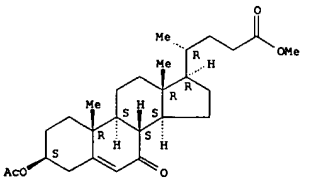
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rotman, Alan L.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Giesser, Joanne M., Winokur, Melvin
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 607
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of the Formula I ##STR1## wherein: the dotted line indicates that a double bond may be present or absent; R.sup.1 is H, methyl or ethyl; R.sup.2 is .alpha.- or .beta.-C.sub.1-10 straight or branched alkyl; R.sup.3 is CO.sub.2 H, CN, CO.sub.2 R.sup.4, CONR.sup.4, or CON(R.sup.4).sub.2 ; R.sup.4 is H, C.sub.1-10 straight or branched alkyl, aryl, heteroaryl, or aralkyl; Aryl is phenyl, substituted phenyl, naphthyl, or biphenyl; Heteroaryl is pyridyl, pyrrolyl, thienyl, furanyl or quinolinyl; and Aralkyl is C.sub.1-10 alkyl substituted with one to three phenyl or substituted phenyl moieties; and their pharmaceutically acceptable salts are described. These compounds are 5.alpha.-reductase type 1 inhibitors. They may be used for treating conditions associated with an excess of DHT, either alone or in combination with other 5.alpha.-reductase inhibitors.

IT **121782-71-6**
(prepn. of azacholanoic acid derivs. as 5.alpha.-reductase inhibitors)
RN 121782-71-6 USPATFULL
CN Chol-5-en-24-oic acid, 3-(acetyloxy)-7-oxo-, methyl ester, (3.beta.)- (9CI) (CA INDEX NAME)

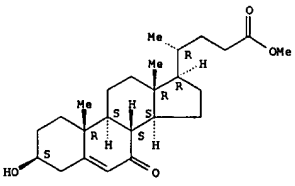
Absolute stereochemistry.

L9 ANSWER 41 OF 75 USPATFULL (Continued)



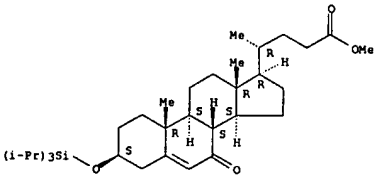
IT **31427-15-3P 178328-79-5P 178328-80-8P**
(prepn. of azacholanoic acid derivs. as 5.alpha.-reductase inhibitors)
RN 31427-15-3 USPATFULL
CN Chol-5-en-24-oic acid, 3-hydroxy-7-oxo-, methyl ester, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 178328-79-5 USPATFULL
CN Chol-5-en-24-oic acid, 7-oxo-3-[[tris(1-methylethyl)silyl]oxy]-, methyl ester, (3.beta.)- (9CI) (CA INDEX NAME)

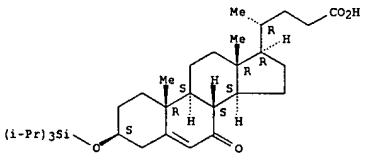
Absolute stereochemistry.



L9 ANSWER 41 OF 75 USPATFULL (Continued)

RN 178328-80-8 USPATFULL
CN Chol-5-en-24-oic acid, 7-oxo-3-[[tris(1-methylethyl)silyl]oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

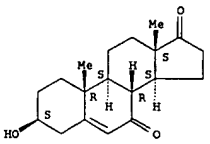


L9 ANSWER 42 OF 75 USPATFULL
ACCESSION NUMBER: 96:116378 USPATFULL
TITLE: Treatment of immune system with .DELTA.5-androstenes
INVENTOR(S): Lardy, Henry A., Madison, WI, United States
PATENT ASSIGNEE(S): Humanetics Corporation, St. Louis Park, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5585371		19961217
APPLICATION INFO.:	US 1994-189917		19940202 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1992-922850, filed on 31 Jul 1992, now patented, Pat. No. US 5292730 which is a continuation-in-part of Ser. No. US 1992-867288, filed on 10 Apr 1992, now patented, Pat. No. US 5296481 which is a continuation of Ser. No. US 1990-575156, filed on 29 Aug 1990, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Criares, Theodore J.
LEGAL REPRESENTATIVE: Sherrill, Michael S.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 596
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Immune system response may be enhanced by administering a .DELTA.5-Androstene-3.beta.-ol-17-one having a C.sub.7 substituent selected from the group consisting of oxo, hydroxy and groups convertible thereto by hydrolysis.
IT **566-19-8P**
(treatment of immune system with .DELTA.5-androstenes)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



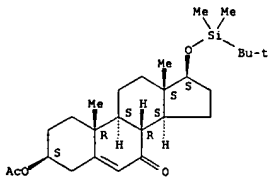
L9 ANSWER 43 OF 75 USPATFULL (Continued)

L9 ANSWER 43 OF 75 USPATFULL
ACCESSION NUMBER: 96:109092 USPATFULL
TITLE: Process for producing 7 .beta.-substituted-4-aza-5 .alpha.-androstan-3-ones
INVENTOR(S): Bakshi, Raman K., Edison, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5578726		19961126
	WO 9323376		19931125
APPLICATION INFO.:	US 1994-335791		19941110 (8)
	WO 1993-US4443		19930511
			19941110 PCT 371 date
			19941110 PCT 102(e) date
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1992-886049, filed on 20 May 1992, now patented, Pat. No. US 5237064		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Giesser, Joanne M., Winokur, Melvin, Fitch, Catherine D.
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 7
LINE COUNT: 654
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Described is a new process for producing 7.beta.-substituted-4-aza-5.alpha.-androstan-3-ones and related compounds which are 5.alpha.-reductase inhibitors, consisting of reducing the corresponding androsteneone with lithium and liquid ammonia, contacting the product with an isomerizing agent, oxidizing the product to a seco acid and reacting that seco acid with an amine to cyclize to form 4-aza-5.alpha.-androstan-3-ones.
IT **151192-86-8P**
(prepn. and Grignard reaction with methylmagnesium chloride)
RN 151192-86-8 USPATFULL
CN Androst-5-en-7-one, 3-(acetyloxy)-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 44 OF 75 USPATFULL
ACCESSION NUMBER: 96:91831 USPATFULL
TITLE: Vaccine compositions and method for enhancing an immune response
INVENTOR(S): Daynes, Raymond A., Park City, UT, United States
Araneo, Barbara A., Salt Lake City, UT, United States
PATENT ASSIGNEE(S): University of Utah Research Foundation, Salt Lake City, UT, United States (U.S. corporation)

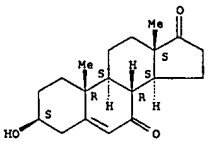
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5562910		19961008
APPLICATION INFO.:	US 1993-123843		19930909 (8)
DISCLAIMER DATE:	20130909		
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-13972, filed on 4 Feb 1993, now abandoned And a continuation-in-part of Ser. No. US 1991-779499, filed on 18 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-412270, filed on 25 Sep 1989, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Housel, James C.
ASSISTANT EXAMINER: Krsek-Staples, Julie
LEGAL REPRESENTATIVE: Venable, Baetjer, Howard & Civiletti, LLP
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 43 Drawing Figure(s); 18 Drawing Page(s)
LINE COUNT: 1591
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a vaccine which comprises an antigen and an immune response augmenting agent. The immune response augmenting agent is capable of enhancing T cell lymphokine production. Suitable immune response augmenting agents include, but are not limited to, dehydroepiandrosterone (DHEA) and DHEA-derivatives. Examples of DHEA derivatives include DHEA-sulfate (DHEA-S), 16.alpha.-bromo-DHEA, 7-oxo-DHEA, 16.alpha.-bromo-DHEA-S and 7-oxo-DHEA-S.

The invention also relates to a method for enhancing a vaccine-induced humoral immune response which comprises administering a vaccine which comprises an antigen and an immunomodulator. The immunomodulator may be an immune response augmenting agent, a lymphoid organ modifying agent or a mixture of the immune response augmenting agent and lymphoid organ modifying agent. Suitable lymphoid organ modifying agents include, but are not limited to, 1,25-dihydroxy Vitamin D.sub.3, biologically active Vitamin D.sub.3 derivatives which are capable of activating the intracellular Vitamin D.sub.3 receptor, all trans-retinoic acid, retinoic acid derivatives, retinol, retinol derivatives and glucocorticoid. Alternatively, the method for enhancing a vaccine-induced humoral immune response comprises separately administering the immunomodulator and a vaccine containing an antigen.
IT **566-19-8 4121-96-4**
(vaccine comprises antigen and immunomodulator or lymphoid organ modifying agent)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

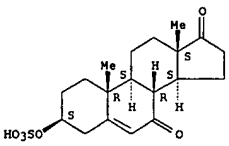
Absolute stereochemistry. Rotation (-).

L9 ANSWER 44 OF 75 USPATFULL (Continued)



RN 4121-96-4 USPATFULL
CN Androst-5-ene-7,17-dione, 3-(sulfooxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



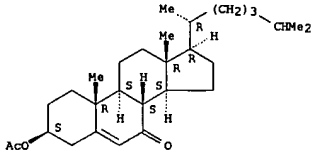
L9 ANSWER 45 OF 75 USPATFULL

ACCESSION NUMBER: 96:70456 USPATFULL
TITLE: Combination method of treating acne using 4-AZA-5.alpha.-cholestan-ones and 4-AZA-5.alpha.-androstan-ones as selective 5.alpha.-reductase inhibitors with anti-bacterial, keratolytic, or anti-inflammatory agents
INVENTOR(S): Waldstreicher, Joanne, Scotch Plains, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5543417		19960806
APPLICATION INFO.:	US 1994-327078		19941021 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Killos, Paul J.
LEGAL REPRESENTATIVE: Fitch, Catherine D., North, Robert J., Winokur, Melvin
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
LINE COUNT: 3981
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Described is a combination method using selective inhibitors of 5.alpha.-reductase 1 and/or 2 including 7.beta.-substituted 4-aza-5.alpha.-cholestan-3-ones and related 4-aza-5.alpha.-androstan-3-one compounds which are useful in the treatment of acne vulgaris in combination with at least one agent selected from an antibacterial, keratolytic, and/or an anti-inflammatory.
IT **809-51-8**
(prepn. of azacholestanones and azaandrostanones as 5.alpha.-reductase inhibitors)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



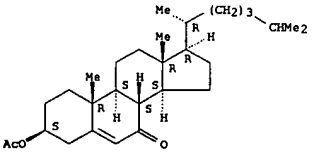
L9 ANSWER 46 OF 75 USPATFULL

ACCESSION NUMBER: 96:53322 USPATFULL
TITLE: 7.beta.-substituted-4-aza-5.alpha.-cholestan-3-ones as 5.alpha. reductase inhibitors useful in the prevention and treatment of hyperandrogenetic disorders
INVENTOR(S): Bakshi, Raman K., Edison, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Patel, Gool F., Millington, NJ, United States
Harris, Georgianna, Tinton Falls, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5527807		19960618
APPLICATION INFO.:	US 1994-335861		19941115 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-886023, filed on 20 May 1992, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Giesser, Joanne M., Fitch, Catherine D.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 961
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Described are new 7.beta.-substituted 4-aza-5.alpha.-cholestan-3-ones and related compounds as 5.alpha.-reductase inhibitors.
IT **809-51-8**
(prepn. of azacholestanones as 5.alpha.-reductase inhibitors)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



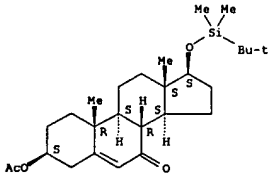
L9 ANSWER 47 OF 75 USPATFULL

ACCESSION NUMBER: 96:50905 USPATFULL
TITLE: 17b-aryl-4-aza-steroid derivatives useful as 5-alpha-reductase inhibitors
INVENTOR(S): Adams, Alan D., Piscataway, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
Steinberg, Nathan G., Clark, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5525608		19960611
APPLICATION INFO.:	US 1994-230277		19940420 (8)

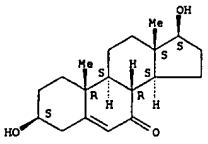
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Quagliato, Carol S., Giesser, Joanne M.
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 1588
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula ##STR1## are inhibitors of 5.alpha.-reductase and are useful alone or in combination with other active agents for the treatment of hyperandrogenic disorders such as acne vulgaris, seborrhea, female hirsutism, male pattern baldness, and benign prostatic hyperplasia.
IT **151192-86-8P**
(prepn. of 17.beta.-arylaza-steroid derivs. as 5.alpha.-reductase inhibitors)
RN 151192-86-8 USPATFULL
CN Androst-5-en-7-one, 3-(acetyloxy)-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



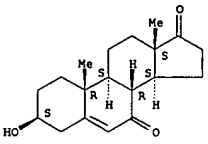
L9 ANSWER 49 OF 75 USPATFULL (Continued)
NAME)

Absolute stereochemistry.



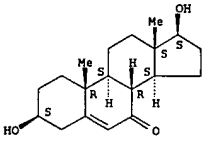
IT **566-19-8D**, esters **2226-65-5D**, esters
(wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

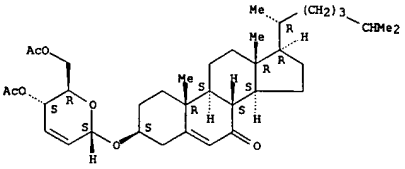


RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 50 OF 75 USPATFULL (Continued)



L9 ANSWER 50 OF 75 USPATFULL
ACCESSION NUMBER: 96:19079 USPATFULL
TITLE: Glycoside compounds and production and use thereof
INVENTOR(S): Klemke, R. Erich, D-70247 Hilzingen, Germany, Federal Republic of
PATENT ASSIGNEE(S): Klemke, R. Erich, Germany, Federal Republic of (non-U.S. individual)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5496806		19960305
APPLICATION INFO.:	US 1994-239373		19940506 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1993-6447, filed on 21 Jan 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-815691, filed on 24 Jan 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-733915, filed on 22 Jul 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-644002, filed on 22 Jan 1991, now patented, Pat. No. US 5278296

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1990-4001895	19900123

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Robinson, Douglas W.
ASSISTANT EXAMINER: Lee, Howard C.
LEGAL REPRESENTATIVE: Young, MacFarlane & Wood
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 412
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel glycosides 7-ketosteryl di-O-acyl-pyranoside and 7-.beta.-hydroxycholesteryl 2,3-dideoxy-.alpha.-D-erythro-hex-2-enopyranoside. The glycosides possess valuable pharmacological properties as a medicament. In particular, the cholesterol glycoside in vivo exhibits a selective cell-destructive activity on malignant cells which activity is substantially free of side effects on normal cells. The glycosides possess useful properties, especially pharmacological properties which are the same as the respective unglycosylated aglycon.
IT **136468-12-7P**
(prepn. and redn. of)
RN 136468-12-7 USPATFULL
CN Cholest-5-en-7-one, 3-[(4,6-di-O-acetyl-2,3-dideoxy-.alpha.-D-erythro-hex-2-enopyranosyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

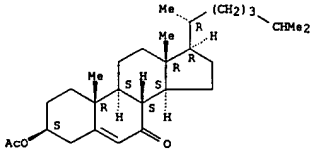
Absolute stereochemistry.

L9 ANSWER 51 OF 75 USPATFULL
ACCESSION NUMBER: 95:105965 USPATFULL
TITLE: Process for the stereoselective reduction of steroid enelactams
INVENTOR(S): Humphrey, Guy R., Belle Mead, NJ, United States
Miller, Ross A., Fanwood, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

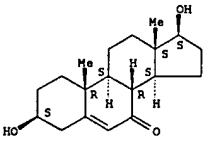
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5470976		19951128
APPLICATION INFO.:	US 1994-301949		19940907 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Quagliato, Carol S.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
LINE COUNT: 795
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The novel process of this invention involves the reduction of certain .DELTA.-5 steroidal alkenes to selectively produce either the 5.alpha. or 5.beta. reduction products. Particularly, this invention involves reduction of .DELTA.-5 steroidal alkenes using a rhodium based catalyst in the presence of hydrogen to selectively yield 5.alpha. steroids or alternatively reduction of .DELTA.-5 steroidal alkenes in an ionizing medium with a trialkylsilane to selectively yield 5.beta. steroids.
IT **809-51-8P**, 7-Oxocholesteryl acetate
(stereoselective redn. of azacholestenones)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

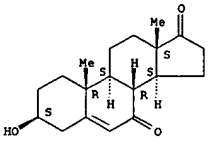


L9 ANSWER 53 OF 75 USPATFULL (Continued)



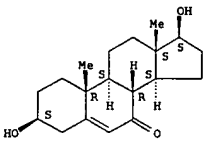
IT **566-19-8D, esters 2226-65-5D, esters**
(wt. loss promotion with)
RN 566-19-8 USPATFULL
CN Androst-5-ene-7,17-dione, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 2226-65-5 USPATFULL
CN Androst-5-en-7-one, 3,17-dihydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 54 OF 75 USPATFULL

ACCESSION NUMBER: 95:11599 USPATFULL
TITLE: Compositions containing corticosteroids or analogues thereof and corticosteroid buffering effective amounts of 5-androstene 3B, 17B or 5-androstene 3B, 7B, 17B triol or analogues thereof
INVENTOR(S): Loria, Roger M., 3819 Brook Rd., Richmond, VA, United States 23227

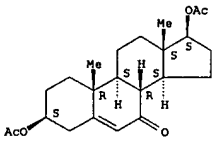
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5387583		19950207
APPLICATION INFO.:	US 1993-50579		19930420 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Dees, Jose G.		
ASSISTANT EXAMINER:	Jones, Dwayne C.		
LEGAL REPRESENTATIVE:	Hendricks, Glenna, Gates, Stephen		
NUMBER OF CLAIMS:	7		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1177		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB 3.beta.,17.beta.-androstenediol (".beta.AED") and 3.beta.,7.beta.,17.beta.-androstenetriol (".beta.AET") may be used to counteract the antiproliferative and immunosuppressive effects of hydrocortisone and other corticosteroids (i.e., to act as buffers to counteract the lymphosuppressive response to such steroids). .beta.AED and .beta.AET are steroids which mediate immune response to provide the body protection against immune down-regulation. A method for testing analogues of .beta.AED and .beta.AET to compare the effectiveness of such analogues as buffers of certain effects of hydrocortisone and other corticosteroids, including immune response and proliferative effects is described. Cytokines, including most particularly IL-3, are produced by addition of .beta.AET and .beta.AED and their analogues to the growth media of cell cultures of lymphatic cells.

IT **13209-60-4P**, 3.beta.,17.beta.-Diacetoxyandros-5-en-7-one
(prepn. and redn. of)
RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 55 OF 75 USPATFULL

ACCESSION NUMBER: 94:93450 USPATFULL
TITLE: 15-substituted 4-azasteroids
INVENTOR(S): Durette, Philippe L., New Providence, NJ, United States
Esser, Craig K., Belford, NJ, United States
Hagmann, William, Westfield, NJ, United States
Kopka, Ihor E., Millburn, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5359071		19941025
APPLICATION INFO.:	US 1993-30508		19930312 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Daus, Donald G.		
LEGAL REPRESENTATIVE:	Giesser, Joanne M., Winokur, Melvin, Matukaitis, Paul D.		
NUMBER OF CLAIMS:	3		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1599		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of the formula ##STR1## or a pharmaceutically acceptable salt or ester thereof, wherein R.sup.1 is selected from the group consisting of hydrogen and C.sub.1-10 alkyl;

R.sup.2 is selected from the group consisting of hydrogen and C.sub.1-10 alkyl;

R.sup.3 is selected from the group consisting of C.sub.1-10 alkoxyl, C.sub.1-10 alkyl and cyano;

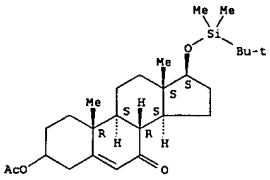
R.sup.4 is selected from the group consisting of C.sub.1-10 alkenyloxyl, C.sub.1-10 alkoxyl, C.sub.1-10 alkyl, C.sub.1-10 alkylcarbamic, C.sub.1-10 alkylcarbonyloxyl, carbonyl, hydroxyl, and --NHR.sup.5, and

R.sup.5 is selected from the group consisting of hydrogen and C.sub.1-10 alkylcarbonyl. Such compounds are useful as selective antagonists of testosterone 5.alpha.-reductase 1.

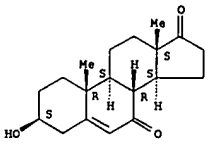
IT **160496-91-3P**
(prepn. of 15-substituted 4-azasteroids as testosterone 5.alpha.-reductase inhibitors)
RN 160496-91-3 USPATFULL
CN Androst-5-en-7-one, 3-(acetyloxy)-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 55 OF 75 USPATFULL (Continued)



L9 ANSWER 57 OF 75 USPATFULL (Continued)



L9 ANSWER 58 OF 75 USPATFULL

ACCESSION NUMBER:	94:3918 USPATFULL
TITLE:	Production of hydroxysteryl glycoside compounds
INVENTOR(S):	Klemke, R.-Erich, Hilzingen, Germany, Federal Republic of
PATENT ASSIGNEE(S):	Gelman Sciences Inc., Ann Arbor, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5278296		19940111
APPLICATION INFO.:	US 1991-644002		19910122 (7)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1990-4001895	19900123

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Husarik, Nancy S.
LEGAL REPRESENTATIVE:	Kraas & Young
NUMBER OF CLAIMS:	9
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT:	504

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel glycosides, especially steroidal glycosides, and a novel method of their production, are provided. For the novel method of producing novel glycosides, hydroxysteryl compounds are glycosylated with tri-O-acyl glucal using molecular iodine as a reaction catalyst. In this method an alcohol or phenol, especially a hydroxy-steroid such as a water-insoluble cholesterol, is glycosylated, such that the glycosylation is performed in a single step. The resulting steryl pyranoside is by oxidation converted to the corresponding 7-ketosteryl di-O-acyl-pyranoside. The latter pyranoside is selectively reduced to provide the corresponding 7-.beta.-hydroxysteryl 2,3-dideoxy-.alpha.-D-erythro-hex-2-enopyranoside. The steroidal glycosides obtained in this way possess valuable pharmacological properties. In particular, the glycosides in vivo exhibit a selective cell-destructive activity on malignant cells which activity is substantially free of side effects on normal cells. The glycosides also possess a drive-enhancing (stimulating) activity and an anti-inflammatory (immunosuppressive or immunoregulatory) activity.

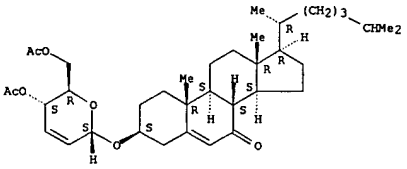
IT **136468-12-7P**
(prepn. and redn. of)

RN 136468-12-7 USPATFULL

CN Cholest-5-en-7-one, 3-[(4,6-di-O-acetyl-2,3-dideoxy-.alpha.-D-erythro-hex-2-enopyranosyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 58 OF 75 USPATFULL (Continued)



L9 ANSWER 59 OF 75 USPATFULL

ACCESSION NUMBER:	94:3531 USPATFULL
TITLE:	Regulation of the immune system
INVENTOR(S):	Loria, Roger M., Richmond, VA, United States
PATENT ASSIGNEE(S):	Virginia Commonwealth University, Richmond, VA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5277907		19940111
APPLICATION INFO.:	US 1992-917720		19920724 (7)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1991-739809, filed on 2 Aug 1991, now patented, Pat. No. US 5206008 which is a continuation-in-part of Ser. No. US 1991-685078, filed on 15 Apr 1991		

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Waddell, Frederick E.
ASSISTANT EXAMINER:	Henley, III, Raymond J.
LEGAL REPRESENTATIVE:	Hendricks, Glenna, Gates, Stephen
NUMBER OF CLAIMS:	8
EXEMPLARY CLAIM:	1
LINE COUNT:	930

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

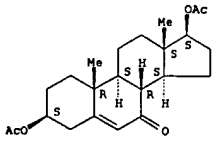
AB The addition of 5-androstene 3.beta.,17.beta.diol and/or 5-androstene 3.beta.,7.beta.,17.beta. triol to growth media increases proliferation of lymphocytes in culture. By methods of the invention it is possible to increase production of autogenous lymphocytes for administration to the patient.

IT **13209-60-4P**, 3.beta., 17.beta.-Diacetoxyandrost-5-en-7-one
(prepn. and reaction of, in immunostimulant androstenetriol prepn.)

RN 13209-60-4 USPATFULL

CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

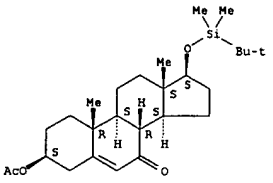


L9 ANSWER 60 OF 75 USPATFULL
ACCESSION NUMBER: 93:67765 USPATFULL
TITLE: Process for producing 7.beta.-substituted-aza-5.alpha.androstan-3-ones
INVENTOR(S): Bakshi, Raman K., Edison, NJ, United States
Rasmusson, Gary H., Watchung, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5237064		19930817
APPLICATION INFO.:	US 1992-886049		19920520 (7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
LEGAL REPRESENTATIVE: Grassler, Frank P., North, Robert J., Caruso, Charles M.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
LINE COUNT: 660
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Described is a new process for producing 7.beta.-substituted-4-aza-5.alpha.-androstan-3-ones and related compounds which are 5.alpha.-reductase inhibitors.
IT **151192-86-8P**
(prepn. and Grignard reaction with methylmagnesium chloride)
RN 151192-86-8 USPATFULL
CN Androst-5-en-7-one, 3-(acetyloxy)-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

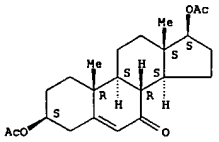


L9 ANSWER 61 OF 75 USPATFULL
ACCESSION NUMBER: 93:33264 USPATFULL
TITLE: Enhancement of immune response
INVENTOR(S): Loria, Roger, Richmond, VA, United States
PATENT ASSIGNEE(S): Virginia Commonwealth University, Richmond, VA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5206008		19930427
APPLICATION INFO.:	US 1991-739809		19910802 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1991-685078, filed on 15 Apr 1991
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Bawa, Raj
LEGAL REPRESENTATIVE: Hendricks, Glenna
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 819
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides an improved means for regulating the immune response, for ameliorating effects of stress, and for avoiding untoward effects of chemotherapy or exposure to irradiation by administration of androstenediol (AED) and androstenetriol (AET). The improved means of regulating immune response can be utilized in treating infectious diseases and immune diseases such as diabetes and chronic fatigue syndrome, both diseases now considered to be immune response related syndromes.
IT **13209-60-4P**
(prepn. and redn. of, in prepn. of isomers of trihydroxyandrostene)
RN 13209-60-4 USPATFULL
CN Androst-5-en-7-one, 3,17-bis(acetyloxy)-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 62 OF 75 USPATFULL
ACCESSION NUMBER: 91:54876 USPATFULL
TITLE: Process for the catalytic oxidation of isoprenoids having allylic groups
INVENTOR(S): Foricher, Joseph, Mulhouse, France
Furbringer, Claude, Riehen, Switzerland
Pfoertner, Karlheinz, Basel, Switzerland
PATENT ASSIGNEE(S): Hoffman-La Roche Inc., Nutley, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5030739		19910709
APPLICATION INFO.:	US 1990-576096		19900831 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1989-453146, filed on 13 Dec 1989, now abandoned which is a continuation of Ser. No. US 1986-849340, filed on 8 Apr 1986, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	CH 1985-1637	19850417

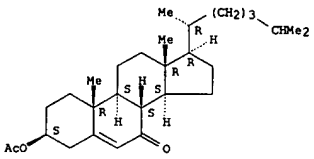
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lee, Mary C.
ASSISTANT EXAMINER: Powers, Fiona T.
LEGAL REPRESENTATIVE: Gould, George M., Leon, Bernard S., Johnston, George W.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 543
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to a process for the catalytic oxidation of an isoprenoid containing at least one allylic hydrogen atom, which process comprises reacting the isoprenoid with oxygen or an oxygen-containing gas in an inert solvent in the presence of a N-hydroxydicarboxylic acid imide of the formula ##STR1## wherein A-B stands for CH.sub.2 -CH.sub.2, CH.dbd.CH, an aromatic hydrocarbon residue or a group derived from one of these groups in which one or more hydrogen atoms is/are replaced by alkyl or halogen,

to produce a primary of secondary hydroperoxide.

The process of the invention is suitable for the manufacture of steroids, vitamins, odorant substances, carotinoids and the like.
IT **809-51-8P**
(prepn. of, by allylic oxidn. of cholesterol acetate)
RN 809-51-8 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 62 OF 75 USPATFULL (Continued)

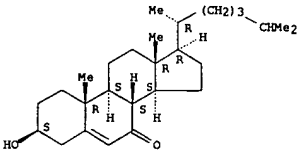


L9 ANSWER 63 OF 75 USPATFULL
ACCESSION NUMBER: 84:20038 USPATFULL
TITLE: Water-soluble cholesterol derivative
INVENTOR(S): Arakawa, Yoshio, 10-18, Ezakacho 1-chome, Suita-shi, Japan
Takanabe, Atsuyuki, 29-19, Nagao-Higashicho 2-chome, Hirakata-shi, Japan
Uemura, Yahiro, 5-18, Mitsuyacho, Hirakata-shi, Japan
Funakoshi, Satoshi, 16-5, Aoyama 1-chome, Katano-shi, Japan
Suyama, Tadakazu, 3-7, Tanabecho, Matsuigaoka 4-chome, Tsuzuki-gun, Kyoto, Japan

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4442037		19840410	
	WO 8203175		19820930	
APPLICATION INFO.:	US 1982-432938		19820928	(6)
	WO 1981-JP56		19810313	
			19820928	PCT 371 date
			19820928	PCT 102(e) date

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 314
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Complexes of albumin combined with organic dibasic acid half esters, such as those of succinic acid and phthalic acid, of 7-hydroxycholesterol are soluble in water and have excellent immunosuppressive and anti-inflammatory action.
IT **566-28-9**
(acylation of, by succinic anhydride)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

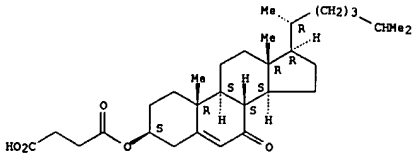
Absolute stereochemistry.



IT **78094-19-6P**
(prepn. and redn. of)
RN 78094-19-6 USPATFULL
CN Cholest-5-en-7-one, 3-(3-carboxy-1-oxopropoxy)-, (3.beta.)- (9CI) (CA

L9 ANSWER 63 OF 75 USPATFULL (Continued)
INDEX NAME)

Absolute stereochemistry.

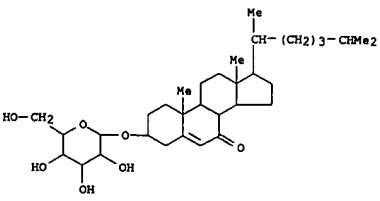


L9 ANSWER 64 OF 75 USPATFULL
ACCESSION NUMBER: 83:39782 USPATFULL
TITLE: Steroid glycoside compounds and methods of use
INVENTOR(S): Matsumura, Shingo, Kyoto, Japan
Enomoto, Hiroshi, Nagaokakyo, Japan
Kitaguchi, Koji, Joyo, Japan
Ozaki, Masakuni, Joyo, Japan
Kitano, Masahiko, Sakyo, Japan
Okamura, Toshihiro, Makishimacho, Japan
Tanaka, Haruo, Hikone, Japan
PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4402948		19830906	
APPLICATION INFO.:	US 1981-227764		19810123	(6)

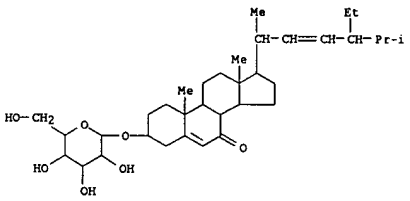
	NUMBER	DATE
PRIORITY INFORMATION:	JP 1980-15308	19800208

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Brown, Johnnie R.
LEGAL REPRESENTATIVE: Jacobs & Jacobs
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1,25
LINE COUNT: 537
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Oxygenated sterylglycoside derivatives of the formula (I) wherein R.sub.1, R.sub.2, R.sub.3 and R.sub.4 are the same or different and each is hydrogen or lower alkanoyl, Y is ##STR1## and R.sub.5 is 4-methylpentyl, 3-ethyl-4-methylpentyl or 3-ethyl-4-methyl-1-pentenyl are useful for their hemostatic and capillary stabilizing effects.
IT **80666-88-2P 80666-90-6P**
(prepn. and hemostatic activity of)
RN 80666-88-2 USPATFULL
CN Cholest-5-en-7-one, 3-(.beta.-D-glucopyranosyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

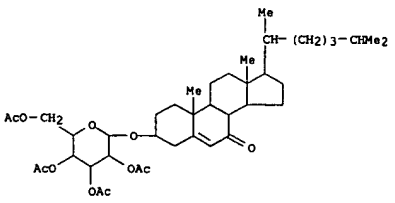


RN 80666-90-6 USPATFULL
CN Stigmasta-5,22-dien-7-one, 3-(.beta.-D-glucopyranosyloxy)-, (3.beta.,22E)- (9CI) (CA INDEX NAME)

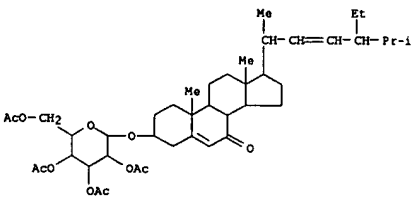
L9 ANSWER 64 OF 75 USPATFULL (Continued)



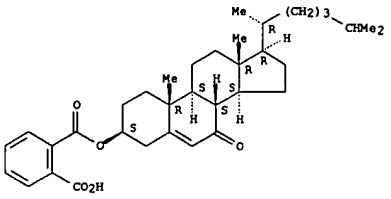
IT **80666-86-0P 80679-02-3P**
(prepn. and redn. of)
RN 80666-86-0 USPATFULL
CN Cholest-5-en-7-one, 3-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (3.beta.)- (9CI) (CA INDEX NAME)



RN 80679-02-3 USPATFULL
CN Stigmasta-5,22-dien-7-one, 3-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (3.beta.,22E)- (9CI) (CA INDEX NAME)



L9 ANSWER 65 OF 75 USPATFULL (Continued)



● Na

L9 ANSWER 66 OF 75 USPATFULL

ACCESSION NUMBER: 81:61542 USPATFULL
TITLE: 25-Alkylcholest-5-ene-3 .beta.,22-diols and esters thereof
INVENTOR(S): Chorvat, Robert J., Arlington Heights, IL, United States
PATENT ASSIGNEE(S): G. D. Searle & Co., Chicago, IL, United States (U.S. corporation)

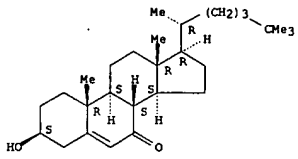
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4299774		19811110
APPLICATION INFO.:	US 1980-145110		19800430 (6)
DISCLAIMER DATE:	19970527		

RELATED APPLN. INFO.: Continuation of Ser. No. US 1978-929068, filed on 28 Jul 1978, now Defensive Publication No. which is a continuation-in-part of Ser. No. US 1977-828385, filed on 29 Aug 1977, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Serauskas, Joy A., Drehkoff, W. Dennis
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 258
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB 25-Alkylcholest-5-ene-3.beta.,22-diols and esters thereof adapted to inhibit the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase are disclosed.

IT **70778-58-4P**
(prepn. and acylation of, by succinic anhydride)
RN 70778-58-4 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

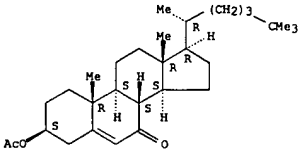
Absolute stereochemistry.



IT **70778-57-3P 71002-47-6P**
(prepn. and deacylation of)
RN 70778-57-3 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

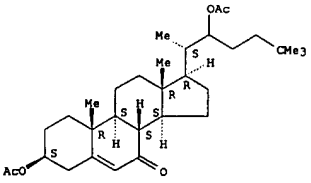
Absolute stereochemistry.

L9 ANSWER 66 OF 75 USPATFULL (Continued)



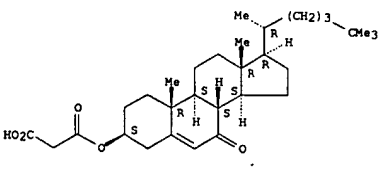
RN 71002-47-6 USPATFULL
CN Cholest-5-en-7-one, 3,22-bis(acetyloxy)-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **70778-68-6P**
(prepn. and selective deesterification of)
RN 70778-68-6 USPATFULL
CN Cholest-5-en-7-one, 3-[(carboxyacetyl)oxy]-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

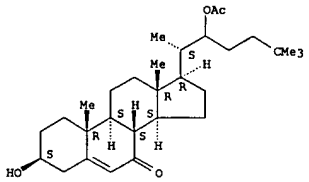
Absolute stereochemistry.



IT **70778-56-2P 70778-59-5P 70778-67-5P**
(prepn. of)
RN 70778-56-2 USPATFULL
CN Cholest-5-en-7-one, 22-(acetyloxy)-3-hydroxy-25-methyl-, (3.beta.)- (9CI)

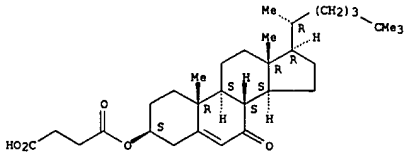
L9 ANSWER 66 OF 75 USPATFULL (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



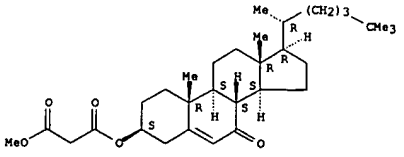
RN 70778-59-5 USPATFULL
CN Cholest-5-en-7-one, 3-(3-carboxy-1-oxopropoxy)-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 70778-67-5 USPATFULL
CN Cholest-5-en-7-one, 3-(3-methoxy-1,3-dioxopropoxy)-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

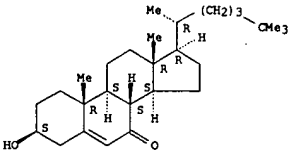


L9 ANSWER 67 OF 75 USPATFULL
ACCESSION NUMBER: 80:13855 USPATFULL
TITLE: 25-Alkyl-3.beta.-hydroxycholest-5-en-7-ones and esters thereof
INVENTOR(S): Chorvat, Robert J., Arlington Heights, IL, United States
PATENT ASSIGNEE(S): G. D. Searle & Co., Skokie, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4193930		19800318
APPLICATION INFO.:	US 1978-928664		19780728 (5)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1977-828385, filed on 29 Aug 1977, now Defensive Publication No.
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Henes, James R., Brown, John M.
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 272
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 25-Alkyl-3.beta.-hydroxycholest-5-en-7-ones and esters thereof adapted to lower serum cholesterol and inhibit the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase are disclosed.
IT **70778-58-4P**
(prepn. and esterification of, with dicarboxylic acid derivs.)
RN 70778-58-4 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

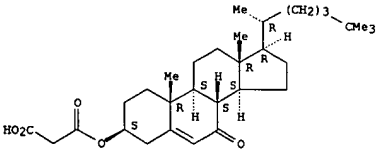


IT **70778-67-5P**
(prepn. and partial hydroxysis of)
RN 70778-67-5 USPATFULL
CN Cholest-5-en-7-one, 3-(3-methoxy-1,3-dioxopropoxy)-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

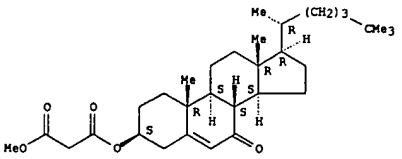
Absolute stereochemistry.

L9 ANSWER 67 OF 75 USPATFULL (Continued)
RN 70778-68-6 USPATFULL
CN Cholest-5-en-7-one, 3-[(carboxyacetyl)oxy]-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

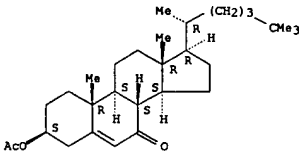


L9 ANSWER 67 OF 75 USPATFULL (Continued)



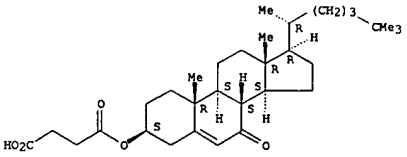
IT **70778-57-3P**
(prepn. and sapon. of)
RN 70778-57-3 USPATFULL
CN Cholest-5-en-7-one, 3-(acetyloxy)-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **70778-59-5P 70778-68-6P**
(prepn. of)
RN 70778-59-5 USPATFULL
CN Cholest-5-en-7-one, 3-(3-carboxy-1-oxopropoxy)-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



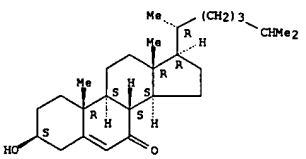
L9 ANSWER 68 OF 75 USPATFULL
ACCESSION NUMBER: 79:27040 USPATFULL
TITLE: Cholesterol derivative-based medicaments acting on bio-protective mechanisms
INVENTOR(S): Kitame, Fumio, Sendai, Japan
Saitoh, Hiroshi, Sendai, Japan
Ishida, Nakao, Sendai, Japan
PATENT ASSIGNEE(S): The Green Cross Corporation, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4157391		19790605
APPLICATION INFO.:	US 1977-804239		19770607 (5)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1977-18939	19770223

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 288
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 7-Hydroxycholesterol and 7-ketocholesterol can be used as a medicament having a pharmacodynamic action on the bio-protective mechanisms, and thus they are useful as an immunoregulatory agent or antiphlogistic agent.
IT **566-28-9P**
(prepn. of, as antiinflammatory and immunosuppressant)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 69 OF 75 USPATFULL

ACCESSION NUMBER:	78:63710 USPATFULL
TITLE:	20/22/23/24-Oxa-7-oxocholesterols and esters thereof
INVENTOR(S):	Dygos, John H., Northbrook, IL, United States
PATENT ASSIGNEE(S):	G. D. Searle, Chicago, IL, United States (U.S. corporation)

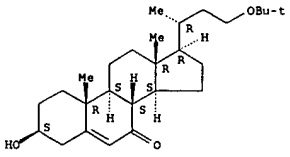
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4125544		19781114
APPLICATION INFO.:	US 1977-804951		19770609 (5)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Brown, John M.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 682
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Preparation and the antimicrobial and antihypercholesterolemic utility of 20/22/23/24-oxa-7-oxocholesterols and esters thereof are disclosed.

IT **69436-63-1P**
(prepn. and acylation of)
RN 69436-63-1 USPATFULL
CN 24-Norchol-5-en-7-one, 23-(1,1-dimethylethoxy)-3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

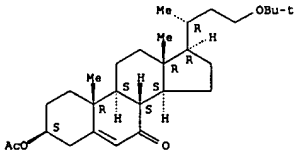
Absolute stereochemistry.



IT **69436-62-0P**
(prepn. and deacetylation of)
RN 69436-62-0 USPATFULL
CN 24-Norchol-5-en-7-one, 3-(acetyloxy)-23-(1,1-dimethylethoxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

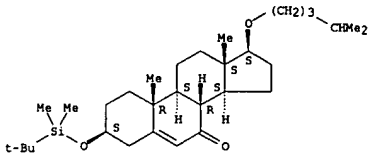
Absolute stereochemistry.

L9 ANSWER 69 OF 75 USPATFULL (Continued)



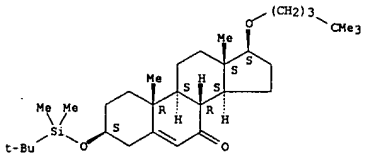
IT **69436-37-9P 69436-40-4P 69436-43-7P 69436-47-1P 69436-51-7P 69436-55-1P 69436-59-5P**
(prepn. and deblocking of)
RN 69436-37-9 USPATFULL
CN Androst-5-en-7-one, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-17-[(4-methylpentyl)oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



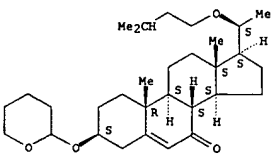
RN 69436-40-4 USPATFULL
CN Androst-5-en-7-one, 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-17-[(4,4-dimethylpentyl)oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



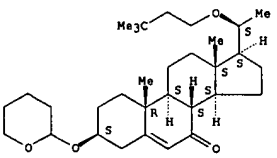
L9 ANSWER 69 OF 75 USPATFULL (Continued)
RN 69436-43-7 USPATFULL
CN Pregn-5-en-7-one, 20-(3-methylbutoxy)-3-[(tetrahydro-2H-pyran-2-yl)oxy]-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



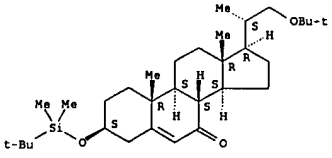
RN 69436-47-1 USPATFULL
CN Pregn-5-en-7-one, 20-(3,3-dimethylbutoxy)-3-[(tetrahydro-2H-pyran-2-yl)oxy]-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 69436-51-7 USPATFULL
CN Pregn-5-en-7-one, 21-(1,1-dimethylethoxy)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-20-methyl-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

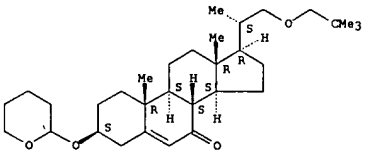
Absolute stereochemistry.



RN 69436-55-1 USPATFULL
CN Pregn-5-en-7-one, 21-(2,2-dimethylpropoxy)-20-methyl-3-[(tetrahydro-2H-

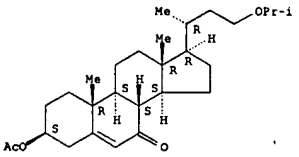
L9 ANSWER 69 OF 75 USPATFULL (Continued)
pyran-2-yl)oxy]-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



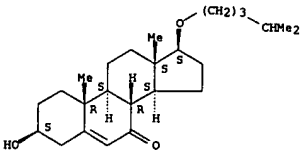
RN 69436-59-5 USPATFULL
CN 24-Norchol-5-en-7-one, 3-(acetyloxy)-23-(1-methylethoxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **67147-65-3P 69436-41-5P 69436-44-8P 69436-48-2P 69436-52-8P 69436-56-2P 69436-60-8P 69436-64-2P**
(prepn. of)
RN 67147-65-3 USPATFULL
CN Androst-5-en-7-one, 3-hydroxy-17-[(4-methylpentyl)oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

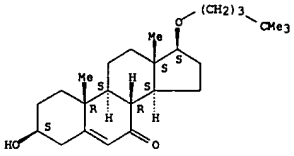
Absolute stereochemistry.



RN 69436-41-5 USPATFULL

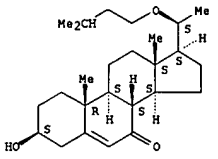
L9 ANSWER 69 OF 75 USPATFULL (Continued)
CN Androst-5-en-7-one, 17-[(4,4-dimethylpentyl)oxy]-3-hydroxy-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



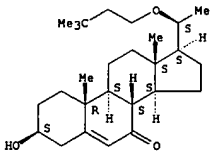
RN 69436-44-8 USPATFULL
CN Pregn-5-en-7-one, 3-hydroxy-20-(3-methylbutoxy)-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 69436-48-2 USPATFULL
CN Pregn-5-en-7-one, 20-(3,3-dimethylbutoxy)-3-hydroxy-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

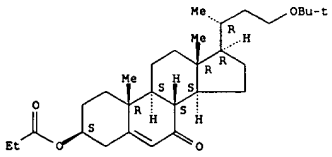
Absolute stereochemistry.



L9 ANSWER 69 OF 75 USPATFULL (Continued)

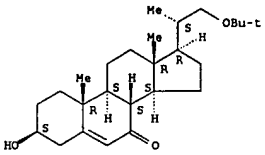
RN 69436-64-2 USPATFULL
CN 24-Norchol-5-en-7-one, 23-(1,1-dimethylethoxy)-3-(1-oxopropoxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



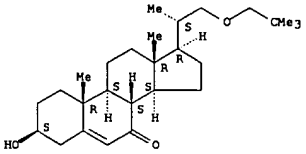
L9 ANSWER 69 OF 75 USPATFULL (Continued)
RN 69436-52-8 USPATFULL
CN Pregn-5-en-7-one, 21-(1,1-dimethylethoxy)-3-hydroxy-20-methyl-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



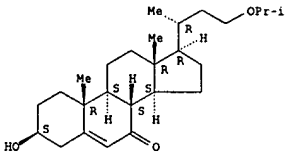
RN 69436-56-2 USPATFULL
CN Pregn-5-en-7-one, 21-(2,2-dimethylpropoxy)-3-hydroxy-20-methyl-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 69436-60-8 USPATFULL
CN 24-Norchol-5-en-7-one, 3-hydroxy-23-(1-methylethoxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 70 OF 75 USPATFULL

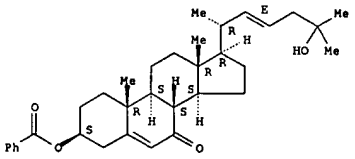
ACCESSION NUMBER:	78:54534 USPATFULL		
TITLE:	Novel method for preparing cholesta-5,7-diene 3.beta.,25-diol and derivatives thereof		
INVENTOR(S):	Salmond, William G., Kalamazoo, MI, United States		
PATENT ASSIGNEE(S):	The Upjohn Company, Kalamazoo, MI, United States (non-U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4116985		19780926
APPLICATION INFO.:	US 1976-708823		19760726 (5)
DISCLAIMER DATE:	19931130		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Roberts, Elbert L.		
LEGAL REPRESENTATIVE:	Barancik, Martin B.		
NUMBER OF CLAIMS:	90		
EXEMPLARY CLAIM:	1		
LINE COUNT:	616		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A new method for synthesizing cholesta-5,7-diene-3.beta.,-25-diol and cholesta-5,7-diene-1.alpha.,3.beta.,25-triol has been discovered. ##STR1## wherein R is hydrogen or hydroxy. Various intermediates and reaction steps are claimed.

IT **66451-98-7P**
(prepn. and reaction of, with benzenesulfonyl hydrazine)
RN 66451-98-7 USPATFULL
CN Cholesta-5,22-dien-7-one, 3-(benzoyloxy)-25-hydroxy-, (3.beta.,22E)- (9CI) (CA INDEX NAME)

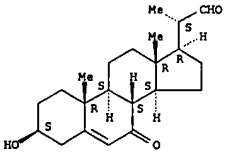
Absolute stereochemistry.
Double bond geometry as shown.



IT **22287-19-0**
(reaction of, with isobutylene oxide and methyltriphenylphosphonium bromide)
RN 22287-19-0 USPATFULL
CN Pregn-5-ene-20-carboxaldehyde, 3-hydroxy-7-oxo-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 70 OF 75 USPATFULL (Continued)



L9 ANSWER 71 OF 75 USPATFULL

ACCESSION NUMBER: 77:23980 USPATFULL
TITLE: Methods and compounds for producing specific antibodies
INVENTOR(S): Gross, Stanley J., Encino, CA, United States
PATENT ASSIGNEE(S): Biological Developments, Inc., Encino, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4022878		19770510
APPLICATION INFO.:	US 1974-528044		19741129 (5)
RELATED APPLN. INFO.:	Division of Ser. No. US 1972-253632, filed on 15 May 1972, now abandoned which is a continuation-in-part of Ser. No. US 1970-45558, filed on 11 Jun 1970, now abandoned And Ser. No. US 1970-89929, filed on 16 Nov 1970, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Padgett, Benjamin R.		
ASSISTANT EXAMINER:	Nucker, Christine M.		
LEGAL REPRESENTATIVE:	McAulay, Fields, Fisher & Goldstein		
NUMBER OF CLAIMS:	8		
EXEMPLARY CLAIM:	1		
LINE COUNT:	774		

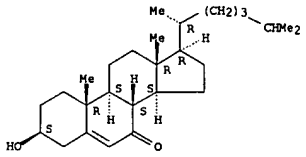
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to a novel method of producing purified antibodies which are truly specific for native homologous hapten or antigen by administering artificial antigens as described therein to an antibody producing host followed by isolation and purification.

IT **566-28-9**
(reaction of, with carboxyphenylhydrazine, antibody prodn. in relation to)

RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 72 OF 75 USPATFULL

ACCESSION NUMBER: 77:6128 USPATFULL
TITLE: Process for 7-keto-.DELTA..sup.5 -steroids
INVENTOR(S): Salmond, William G., Kalamazoo, MI, United States
PATENT ASSIGNEE(S): The Upjohn Company, Kalamazoo, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4006172		19770201
APPLICATION INFO.:	US 1976-680022		19760426 (5)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Roberts, Elbert L.		
LEGAL REPRESENTATIVE:	Stein, Bruce, Saliwanchik, Roman		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		
LINE COUNT:	224		

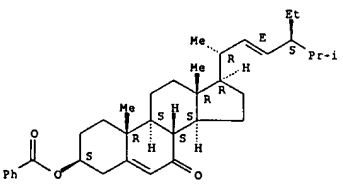
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is an improved process for the oxidation of certain .DELTA..sup.5 -steroids to the corresponding 7-keto-.DELTA..sup.5 -steroids by use of a chromium trioxide-pyrazole oxidant (oxidizing agent).

IT **62301-73-9P**
(prepn. of)

RN 62301-73-9 USPATFULL
CN Stigmasta-5,22-dien-7-one, 3-(benzoyloxy)-, (3.beta.,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L9 ANSWER 73 OF 75 USPATFULL

ACCESSION NUMBER: 76:36702 USPATFULL
TITLE: Process for the production of 1.alpha.-hydroxy provitamin D.sub.3 and 1.alpha.-hydroxy vitamin D.sub.3
INVENTOR(S): Mazur, Yehuda, Tel-Aviv, Israel
Freeman, Dalia, Rishon Lezion, Israel
Acher, Aureliu J., Ramat-Gan, Israel
PATENT ASSIGNEE(S): Yeda Research & Development Co. Ltd., Rehovot, Israel (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3966777		19760629
APPLICATION INFO.:	US 1975-622647		19751015 (5)

	NUMBER	DATE
PRIORITY INFORMATION:	IL 1974-45897	19741022
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Roberts, Elbert L.	
LEGAL REPRESENTATIVE:	Browdy and Neimark	
NUMBER OF CLAIMS:	16	
EXEMPLARY CLAIM:	1,8	
LINE COUNT:	252	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

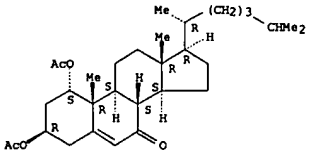
AB A process for the production of 1.alpha.-hydroxy provitamin D.sub.3 which comprises treating 1.alpha., 2.alpha.-epoxy-cholesta-4,6-diene-3-one at a low temperature with liquid ammonia; with ammonium chloride and with lithium metal to produce 1.alpha.,3.beta.-dihydroxycholest-6-ene, converting this to the corresponding 1.alpha.,3.beta.-di(lower alkanoyl) derivative, reacting the latter with bromine to give 1.alpha.,3.beta.-di(lower alkanoyloxy) 6.beta.,7.alpha.-dibromocholestane, which is dehydrobrominated to give 1.alpha.,3.beta.-di(lower alkanoyloxy)-cholesta-5,7-diene, which is converted to the desired provitamin. The 1.alpha.,3.beta.-di(lower alkanoyloxy)cholest-6-ene can be oxidized to the corresponding 5-ene-7-one, which is converted to the 7-p-toluenesulfonyl hydrazone derivative, which is converted to the 1.alpha.-hydroxy provitamin D.sub.3 di(lower alkanoyloxy) derivative or to the 1.alpha.-hydroxy provitamin D.sub.3. Novel compounds are 1.alpha.,3.beta.-dihydroxy-cholest-6-ene, its di(lower alkanoyloxy) derivative; 1.alpha.,3.beta.-di(lower alkanoyloxy)-6.beta.,7.alpha.-dibromocholestane; 1.alpha.,3.beta.-diacetoxycholest-5-ene-7-one and the corresponding 7-p-toluenesulfonylhydrazone derivative.

IT **60008-81-3P**
(prepn. and reaction of, with tosylhydrazide)

RN 60008-81-3 USPATFULL
CN Cholest-5-en-7-one, 1,3-bis(acetyloxy)-, (1.alpha.,3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 73 OF 75 USPATFULL (Continued)



L9 ANSWER 74 OF 75 USPATFULL

ACCESSION NUMBER: 76:32169 USPATFULL
TITLE: 7-Oxa steroids
INVENTOR(S): Guthrie, Robert William, Fairfield, NJ, United States
Kierstead, Richard Wightman, North Caldwell, NJ, United States
Lemahieu, Ronald Andrew, North Caldwell, NJ, United States
PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)

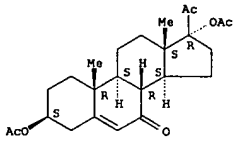
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3962275		19760608
APPLICATION INFO.:	US 1974-531494		19741211 (5)
RELATED APPLN. INFO.:	Division of Ser. No. US 1972-259526, filed on 5 Jun 1972, now patented, Pat. No. US 3869467		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Moyer, Donald B.
LEGAL REPRESENTATIVE: Welt, Samuel L., Leon, Bernard S., Epstein, William H.
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 1110
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB 7-Oxa steroids which may be substituted in the 3-position with a hydroxy or oxo group or in the 2-position with a hydroxymethylene group or in the 2- and 3-positions with a substituent that forms a 5-membered heterocyclic ring, useful as antigonadotropic agents and a method of preparing these 7-oxa steroids from 3-hydroxy .DELTA..sup.5 -steroids including intermediates in this process.

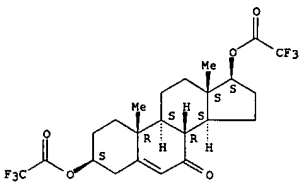
IT **13258-29-2**
(hydrogenation of)
RN 13258-29-2 USPATFULL
CN Pregn-5-ene-7,20-dione, 3,17-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **60273-33-8P**
(prepn. and hydrogenation-hydrolysis of)
RN 60273-33-8 USPATFULL
CN Androst-5-en-7-one, 3,17-bis[(trifluoroacetyl)oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

L9 ANSWER 74 OF 75 USPATFULL (Continued)
Absolute stereochemistry.



L9 ANSWER 75 OF 75 USPATFULL

ACCESSION NUMBER: 75:11192 USPATFULL
TITLE: 17-.beta.-Hydroxy-17-.alpha.-methyl-5-.alpha.-androstano]3,2-c]or[2,3-d]isoxazoles
INVENTOR(S): Guthrie, Robert William, Fairfield, NJ, United States
Kierstead, Richard Wightman, North Caldwell, NJ, United States
LeMahieu, Ronald Andrew, North Caldwell, NJ, United States
PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)

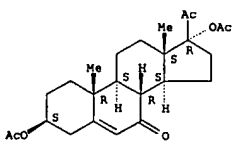
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3869467		19750304
APPLICATION INFO.:	US 1972-259526		19720605 (5)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
ASSISTANT EXAMINER: McCloud, Ralph D.
LEGAL REPRESENTATIVE: Welt, Samuel L., Saxe, Jon S., Epstein, William H.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
LINE COUNT: 1107
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB 7-Oxa steroids which may be substituted in the 3-position with a hydroxy or oxo group or in the 2-position with a hydroxymethylene group or in the 2- and 3-positions with a substituent that forms a 5-membered heterocyclic ring, useful as antigonadotropic agents and a method of preparing these 7-oxa steroids from 3-hydroxy .DELTA..sup.5 -steroids including intermediates in this process.

IT **13258-29-2**
(hydrogenation of)
RN 13258-29-2 USPATFULL
CN Pregn-5-ene-7,20-dione, 3,17-bis(acetyloxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

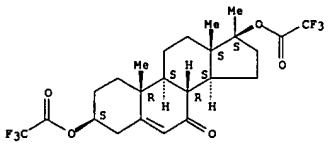
Absolute stereochemistry.



IT **40497-33-4P**
(prepn. and hydrogenation of)
RN 40497-33-4 USPATFULL
CN Androst-5-en-7-one, 17-methyl-3,17-bis[(trifluoroacetyl)oxy]-, (3.beta.,17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 75 OF 75 USPATFULL (Continued)

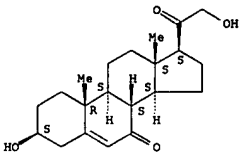


```
=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   397.73     723.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -25.40

FILE 'REGISTRY' ENTERED AT 15:51:46 ON 19 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:   18 AUG 2002  HIGHEST RN 444143-77-5
DICTIONARY FILE UPDATES:  18 AUG 2002  HIGHEST RN 444143-77-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 128a.str

L10     STRUCTURE UPLOADED

=> d his

     (FILE 'HOME' ENTERED AT 15:37:32 ON 19 AUG 2002)

     FILE 'REGISTRY' ENTERED AT 15:37:37 ON 19 AUG 2002
L1              STRUCTURE UPLOADED
L2            4 S L1
L3              STRUCTURE UPLOADED
L4            3 S L3
L5          627 S L3 FULL

     FILE 'CAPLUS' ENTERED AT 15:40:30 ON 19 AUG 2002
L6         1470 S L5
L7           41 S L5/THU

     FILE 'USPATFULL' ENTERED AT 15:43:12 ON 19 AUG 2002
L8           90 S L5
L9           75 S L8 NOT PY>=2001

     FILE 'REGISTRY' ENTERED AT 15:51:46 ON 19 AUG 2002
L10             STRUCTURE UPLOADED

=> s l10 sub=l5 full
```

```
FULL SUBSET SEARCH INITIATED 15:52:12 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -    627 TO ITERATE

100.0% PROCESSED     627 ITERATIONS                          142 ANSWERS
SEARCH TIME: 00.00.04

L11          142 SEA SUB=L5 SSS FUL L10

=> d scan
```

L11 142 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Pregn-5-ene-7,20-dione, 3.beta.,21-dihydroxy- (6CI)
MF C21 H30 O4

Absolute stereochemistry.



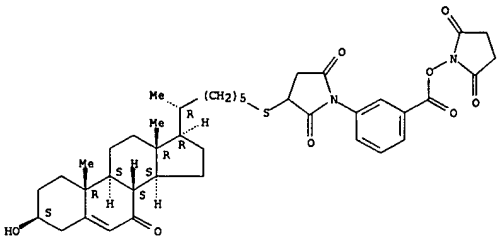
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

```
=> s l11 and 1/s
       3354096 1/S
L12           4 L11 AND 1/S

=> d scan
```

L12 4 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2,5-Pyrrolidinedione, 1-[3-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]phenyl]-3-[[(3.beta.)-3-hydroxy-7-oxo-27-norcholest-5-en-26-yl]thio]- (9CI)
MF C41 H52 N2 O8 S

Absolute stereochemistry.

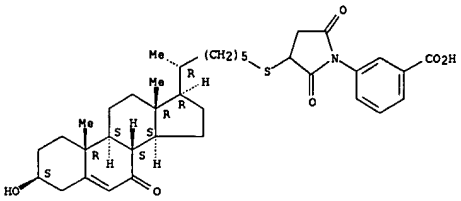


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L12 4 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzoic acid, 3-[3-[[(3.beta.)-3-hydroxy-7-oxo-27-norcholest-5-en-26-yl]thio]-2,5-dioxo-1-pyrrolidinyl]- (9CI)
MF C37 H49 N O6 S

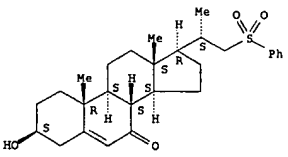
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 4 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Pregn-5-en-7-one, 3-hydroxy-20-methyl-21-(phenylsulfonyl)-, (3.beta.,20S)- (9CI)
MF C28 H38 O4 S

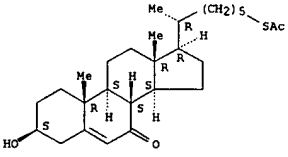
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 4 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 27-Norcholest-5-en-7-one, 26-(acetylthio)-3-hydroxy-, (3.beta.)- (9CI)
MF C28 H44 O3 S

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

```
=> d his

     (FILE 'HOME' ENTERED AT 15:37:32 ON 19 AUG 2002)

     FILE 'REGISTRY' ENTERED AT 15:37:37 ON 19 AUG 2002
L1             STRUCTURE UPLOADED
L2           4 S L1
L3             STRUCTURE UPLOADED
L4           3 S L3
L5         627 S L3 FULL

     FILE 'CAPLUS' ENTERED AT 15:40:30 ON 19 AUG 2002
L6        1470 S L5
L7          41 S L5/THU

     FILE 'USPATFULL' ENTERED AT 15:43:12 ON 19 AUG 2002
L8          90 S L5
L9          75 S L8 NOT PY>=2001

     FILE 'REGISTRY' ENTERED AT 15:51:46 ON 19 AUG 2002
L10            STRUCTURE UPLOADED
L11       142 S L10 FULL SUB=L5
L12         4 S L11 AND 1/S

=> del l12 y

=> file caplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                37.81     761.11

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                 0.00     -25.40

FILE 'CAPLUS' ENTERED AT 15:53:11 ON 19 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 19 Aug 2002  VOL 137 ISS 8
FILE LAST UPDATED: 18 Aug 2002  (20020818/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
```

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> s l11
L12         1017 L11

=> s l11/thu
            1017 L11
          457094 THU/RL
L13           17 L11/THU
                   (L11 (L) THU/RL)

=> d ibib ab hitstr 1-17
```

L13 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:167790 CAPLUS
DOCUMENT NUMBER: 134:217169
TITLE: Oxysterols for modulating HDL cholesterol and triglyceride levels by modulating LXR-mediated transcription
INVENTOR(S): Hayden, Michael R.; Brooks-Wilson, Angela R.; Pimstone, Simon N.; Clee, Susanne M.
PATENT ASSIGNEE(S): University of British Columbia, Can.; Xenon Genetics, Inc.
SOURCE: PCT Int. Appl., 316 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015676	A2	20010308	WO 2000-IB1492	20000901
WO 2001015676	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-151977P P 19990901
US 2000-526193 A 20000315
US 2000-213958P P 20000623

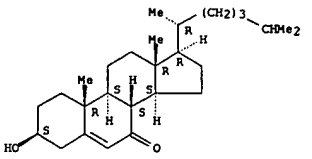
AB The invention features methods for treating patients having low HDL, a higher than normal triglyceride level, or a cardiovascular disease by administering compds. that modulate ABC1 expression or activity. Compds. of the invention include oxysterols that modulate LXR-mediated transcription.

IT **566-28-9**, 7-Oxocholesterol **220066-66-0**, 7-Oxo-24(S),25-epoxycholesterol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(oxysterols for modulating HDL cholesterol and triglyceride levels by modulating LXR-mediated transcription)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

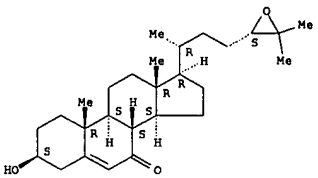
Absolute stereochemistry.

L13 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 220066-66-0 CAPLUS
CN Cholest-5-en-7-one, 24,25-epoxy-3-hydroxy-, (3.beta.,24S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



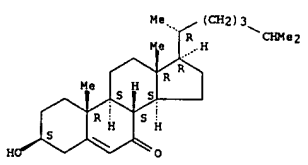
L13 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:87328 CAPLUS
DOCUMENT NUMBER: 135:17931
TITLE: Comparative analysis of plasma and erythrocyte 7-ketocholesterol as a marker for oxidative stress in patients with diabetes mellitus
AUTHOR(S): Abo, Katsumi; Mio, Takaya; Sumino, Kimiaki
CORPORATE SOURCE: Department of Public Health, Kobe University School of Medicine, Kobe, 650-0017, Japan
SOURCE: Clinical Biochemistry (2000), 33(7), 541-547
CODEN: CLBIAS; ISSN: 0009-9120
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objectives: To reveal increased lipid peroxidn. in diabetics by quantification of cholesterol oxidn. products (COPs) not only in plasma, but also in erythrocytes. Design and methods: We quantified 7-ketocholesterol (7-kCho) by gas chromatog.-mass spectrometry as a surrogate measure for COPs. These assays were performed on both plasma and erythrocytes in 20 control subjects and 20 treated patients with relatively poorly controlled Type 2 diabetes. Results: Both plasma and erythrocyte 7-kCho levels in diabetics were significantly higher than those in control subjects. Although neither plasma nor erythrocyte 7-kCho levels were assocd. with markers for glucose tolerance in diabetics, a neg. correlation of serum HDL-cholesterol levels with erythrocyte, but not plasma, 7-kCho levels was found. Conclusion: Increased oxidative stress in diabetics affects oxidn. of cholesterol. Assays of COPs not only in plasma, but also in erythrocytes, may yield complementary information in lipid peroxidn.

IT **566-28-9**, 7-Ketocholesterol
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(comparative anal. of plasma and erythrocyte 7-ketocholesterol as a marker for oxidative stress in human patients with diabetes mellitus)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:412729 CAPLUS
DOCUMENT NUMBER: 133:133759
TITLE: Cholesterol movement in Niemann-Pick type C cells and in cells treated with amphiphiles
AUTHOR(S): Lange, Yvonne; Ye, Jin; Rigney, Mike; Steck, Theodore
CORPORATE SOURCE: Department of Pathology, Rush-Presbyterian-St. Luke's Medical Center, University of Chicago, Chicago, IL, 60637, USA
SOURCE: Journal of Biological Chemistry (2000), 275(23), 17468-17475
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

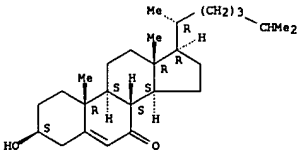
AB Cholesterol accumulates to massive levels in cells from Niemann-Pick type C (NP-C) patients and in cells treated with class 2 amphiphiles that mimic NP-C disease. This behavior has been attributed to the failure of cholesterol released from ingested low d. lipoproteins to exit the lysosomes. However, the authors now show that the rate of movement of cholesterol from lysosomes to plasma membranes in NP-C cells is at least as great as normal, as was also found previously for amphiphile-treated cells. Furthermore, the lysosomes in these cells filled with plasma membrane cholesterol in the absence of lipoproteins. In addn., the authors showed that the size of the endoplasmic reticulum cholesterol pool and the set point of the homeostatic sensor of cell cholesterol were approx. normal in NP-C cells. The plasma membrane cholesterol pools in both NP-C and amphiphile-treated cells were also normal. Furthermore, the build up of cholesterol in NP-C lysosomes was not a physiol. response to cholesterol overload. Rather, it appeared that the accumulation in NP-C lysosomes results from an imbalance in the brisk flow of cholesterol among membrane compartments. In related expts., the authors found that NP-C cells did not respond to class 2 amphiphiles (e.g. trifluoperazine, imipramine, and U18666A); these agents may therefore act directly on the NPC1 protein or on its pathway. Finally, the authors showed that the lysosomal cholesterol pool in NP-C cells was substantially and preferentially reduced by incubating cells with the oxysterols, 25-hydroxycholesterol and 7-ketocholesterol; these findings suggest a new pharmacol. approach to the treatment of NP-C disease.

IT **566-28-9**, 7-Ketocholesterol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lysosomal cholesterol pool in human Niemann-Pick type C cells was substantially and preferentially reduced by incubating cells with oxysterols, 25-hydroxycholesterol and 7-ketocholesterol)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

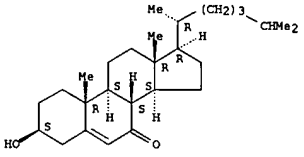
Absolute stereochemistry.

L13 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:243980 CAPLUS
DOCUMENT NUMBER: 133:15832
TITLE: Plasma oxysterols and tocopherol in patients with diabetes mellitus and hyperlipidemia
AUTHOR(S): Murakami, Hiroshi; Tamasawa, Naoki; Matsui, Jun; Yasujima, Minoru; Suda, Toshihiro
CORPORATE SOURCE: Third Department of Internal Medicine, Hirosaki University School of Medicine, Hirosaki, 036-8562, Japan
SOURCE: Lipids (2000), 35(3), 333-338
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The plasma levels of free oxysterols (7-ketocholesterol; 7.alpha.-hydroxy-,7.beta.-hydroxy-, 25-hydroxy-, and 27-hydroxycholesterol; and 5.alpha.,6.alpha.-epoxycholestanol) in patients with diabetes mellitus and hypercholesterolemia were detd. using gas chromatog.-mass spectrometry with selective ion monitoring. We studied 39 patients with diabetes mellitus, 20 nondiabetic patients with hypercholesterolemia, and 37 normal controls. Plasma cholesterol levels in diabetic and hypercholesterolemic patients showed no statistical difference. Plasma 7-ketocholesterol was significantly higher in patients with diabetes (31.6 .+-. 2.8 ng/mL) or hypercholesterolemia (52.3 .+-. 5.9) than in the control group (22.4 .+-. 1.2). The increased plasma cholesterol can be regarded as an oxidn. substrate for the oxidant stress and the higher abs. levels of oxysterols in hypercholesterolemic plasma compared with the control plasma. This difference disappeared when 7-ketocholesterol was expressed in proportion to total cholesterol. The oxidizability of plasma cholesterol was evaluated by comparing the increased ratio of 7-ketocholesterol after CuSO4 oxidn. to the ratio before. We demonstrated that the patients with diabetes showed increased oxidizability (77.5%) compared with the control (36.6%) or hyperlipemic group (45.3%), which is likely due to the lower amts. of .alpha.-tocopherol in the diabetics. Measurement of oxysterols may serve as a marker for in vivo oxidized lipoproteins in diabetes and hyperlipemia.

IT **566-28-9**, 7-Ketocholesterol
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(oxysterols and tocopherol in human plasma in diabetes mellitus and hyperlipidemia as marker of oxidn.)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2002 ACS

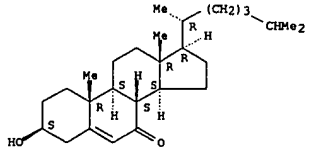
ACCESSION NUMBER: 2000:237584 CAPLUS
DOCUMENT NUMBER: 133:125256
TITLE: Analysis of 7-ketocholesterol in low density lipoprotein and fatty acid composition in erythrocyte membranes of patients on maintenance hemodialysis and healthy controls
AUTHOR(S): Tsuzuki, D.; Sumino, K.; Yokoyama, M.
CORPORATE SOURCE: Department of Public Health, Kobe University, School of Medicine, Kobe, Hyogo, Japan
SOURCE: Clinica Chimica Acta (2000), 295(1-2), 155-168
CODEN: CCATAR; ISSN: 0009-8981
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We established a method to quantify 7-ketocholesterol (7-KC) in low d. lipoprotein by using the heparin-citrate method and gas chromatog.-mass spectrometry. We examd. the concn. of 7-ketocholesterol in LDL using this method to assess the pathol. conditions in uremic patients with hemodialysis and healthy controls. We also examd. the fatty acid compn. in erythrocyte membranes to est. the modification of biol. membranes. We showed that the concns. of 7-KC/cholesterol in LDL were significantly increased in hemodialysis patients compared to healthy controls (3.68.+-.0.45 vs. 2.41.+-.0.19, P<0.05) and the ratio of polyunsatd. fatty acids to satd. fatty acids in erythrocyte membranes was significantly decreased in hemodialysis patients compared to healthy controls (0.499.+-.0.014 vs. 0.655.+-.0.017, P<0.001). There was no significant difference in 7-KC concn. in LDL or fatty acid compn. in erythrocyte membranes between pre- and post-intervention of hemodialysis. We concluded that hemodialysis patients are under oxidative stress, which modifies LDL and erythrocyte membranes and we speculated these modifications may participate in the process of atherosclerosis. We believe that the method to quantify 7-KC in this study is concise and reliable and may be used to investigate various diseases.

IT **566-28-9**, 7-Ketocholesterol
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(anal. of 7-ketocholesterol in LDL and fatty acid compn. in erythrocyte membranes of patients on maintenance hemodialysis and healthy controls)

RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

L13 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2002 ACS

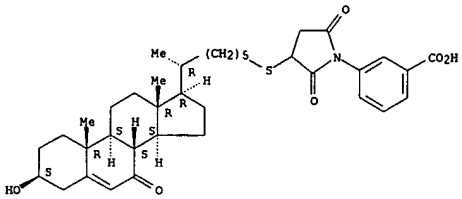
ACCESSION NUMBER: 2000:51386 CAPLUS
DOCUMENT NUMBER: 132:262320
TITLE: Utility of i-steroid-route to oxidized sterol bound to a cross-linker: synthesis of the steroid antigen
AUTHOR(S): Kim, Byung Ju; Morita, Hiroyuki
CORPORATE SOURCE: Department of System Engineering of Materials and Life Science, Faculty of Engineering, Toyama University, Toyama, 930-8555, Japan
SOURCE: Chemistry Letters (2000), (1), 42-43
CODEN: CMLTAG; ISSN: 0366-7022
PUBLISHER: Chemical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The target sterol, which was for prepn. of oxidized sterol antigen to apply to a new antibody diagnostic method for circulatory disease, was successfully synthesized via i-steroid transformation as followings: (1) the Grignard reaction, (2) Barton-McCombie reaction, (3) regioselective photolytic-addn. of thiolacetic acid toward 25-double bond, and (4) in situ Michael addn. between the thiol and a cross-linker.

IT **263356-67-8DP**, conjugate with keyhole limpet protein
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(utility of i-steroid-route to oxidized sterol bound to a cross-linker for the synthesis of steroid antigen)

RN 263356-67-8 CAPLUS
CN Benzoic acid, 3-[3-[[(3.beta.)-3-hydroxy-7-oxo-27-norcholest-5-en-26-yl]thio]-2,5-dioxo-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2002 ACS

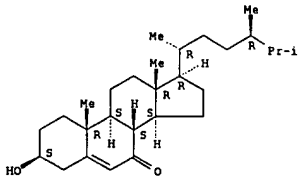
ACCESSION NUMBER: 1999:493647 CAPLUS
DOCUMENT NUMBER: 132:113143
TITLE: Phytosterol oxides in some samples of pure phytosterols mixture and in a few tablet supplement preparations in Finland
AUTHOR(S): Dutta, Paresh C.
CORPORATE SOURCE: Department of Food Science, Swedish University of Agricultural Sciences, Uppsala, 750 07, Swed.
SOURCE: Special Publication - Royal Society of Chemistry (1999), 240(Natural Antioxidants and Anticarcinogens in Nutrition, Health and Disease), 316-319
CODEN: SROCDO; ISSN: 0260-6291
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Detns. were made of polar oxidn. products of phytosterols in raw materials (wood sterols) and in a no. of supplement tablet prepns. contg. photosterols com. available in Finland. In addn., a sample of pure phytosterol mixt. was subjected to oxidn. by treatment at high temp. was analyzed and compared with the unheated raw materials. The content of total polar oxidized sterols in the wood sterols and recrystd. sterols were 75 mg/100g and 44 mg/100g, resp., whereas the heat-treated sterols had 1380 mg/100g. The table prepns. Anti K-steroli, Tri Tolosen Kasvisteroli, and Kolestop (trade names fro com. phytosterol supplement products) had the total polar oxidn. products of 14 mg/100 g, 26 mg/100 g, and 30 mg/100 g tablets, resp. Only 6 of the polar oxidn. products were identified by GC-MS by comparing the mass spectra with those of authentic samples. Among the polar oxidized phytosterols identified, the highest amts. obsd. were epimers of epoxycampesterol and sitosterol, and 7-ketocampesterol and sitosterol. In the tablet prepns, amts. of epoxysterols ranged 5-14 mg/100 g, and 7-ketosterols ranged 3-5 mg/100g.

IT **55396-22-0**, 7-Ketocampesterol
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(phytosterol oxides in pure phytosterol mixts. and in tablet supplement prepns. in Finland)

RN 55396-22-0 CAPLUS
CN Ergost-5-en-7-one, 3-hydroxy-, (3.beta.,24R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

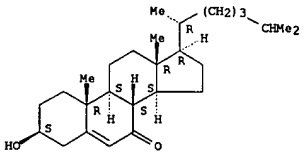
L13 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

L13 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:417233 CAPLUS
DOCUMENT NUMBER: 129:156591
TITLE: Inhibition of p42/p44 mitogen-activated protein kinase by oxysterols in rat astrocyte primary cultures and C6 glioma cell lines
AUTHOR(S): Adamczyk, Monika; Scherrer, Elisabeth; Kupferberg, Alexandre; Malviya, Anant N.; Mersel, Marcel
CORPORATE SOURCE: Centre of Neurochemistry, CNRS, Strasbourg, Fr.
SOURCE: Journal of Neuroscience Research (1998), 53(1), 38-50
CODEN: JNREDK; ISSN: 0360-4012
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We previously demonstrated that oxysterols inhibit the growth of exptl. glioblastoma induced in the rat brain cortex. Mechanism of action of these compds. remains obscure. In this study, we investigated the effect of 7.beta.-hydroxycholesterol (7.beta.-OHCH) and 7-ketocholesterol (7k-CH) on the growth and MAP kinase activity in three in vitro biol. models: rat astrocyte primary cultures, primary cultures treated by dibutyryl-cAMP (reactive cells), and the C6 glioma cell line. The oxysterols are not lethal to primary astrocytes, even if MAP kinase activity is decreased, particularly when cells were treated with 7k-CH. Both oxysterols are toxic to reactive astrocytes, and as compared with untreated primary cultures, they amplified the MAP kinase activity decrease. However, the mechanism of action of oxysterols on reactive astrocytes seems not to be linked to the MAP kinase pathway. In highly proliferating C6 cell lines, only 7.beta.-OHCH has an antiproliferative effect and is cytotoxic. The inhibition of MAP kinase activity is a function of 7.beta.-OHCH concn. PD098059, a MAP kinase pathway inhibitor, has only a time-limited antiproliferative effect on C6 cell growth. We conclude that in C6 cells, the MAP kinase activity decrease is correlated with the toxic effect of 7.beta.-OHCH and occurs at first stages of 7.beta.-OHCH action.

IT **566-28-9**, 7-Ketocholesterol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibition of p42/p44 mitogen-activated protein kinase by oxysterols in rat astrocyte primary cultures and C6 glioma cell lines)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



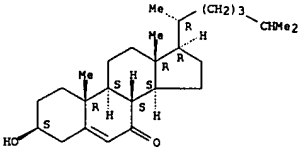
L13 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)

L13 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:433949 CAPLUS
DOCUMENT NUMBER: 127:117127
TITLE: Evaluation of the cytotoxic effects of some oxysterols and of cholesterol on endothelial cell growth: methodological aspects
AUTHOR(S): Lizard, G.; Gueldry, S.; Deckert, V.; Gambert, P.; Lagrost, L.
CORPORATE SOURCE: INSERM-CJF 93/10, Laboratoire de Biochimie Medicale, Hopital de Bocage, Dijon, 21034, Fr.
SOURCE: Pathologie Biologie (1997), 45(4), 281-290
CODEN: PTBIAN; ISSN: 0031-3009
PUBLISHER: Expansion Scientifique Francaise
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of various oxysterol (7.beta.-hydroxycholesterol, 7-ketocholesterol, 19-hydroxycholesterol, cholesterol-5.alpha.,6.alpha.-epoxide, and 25-hydroxycholesterol) and of cholesterol were investigated on cell growth of bovine aortic endothelial (BAE) cells by cell counting, MTT redn., and 3H-thymidine incorporation in a 5 to 80 .mu.g/mL concn. range. By cell counting, a dose related decrease in the no. of adherent cells was obsd. with oxysterols; MTT redn. also indicated a decreased no. of viable cells, and both method give similar IC50. A lower 3H-thymidine incorporation was generally detected with oxysterols but no effect on 3H-thymidine incorporation was found with 25-hydroxycholesterol. With cholesterol, no modification of cell growth was shown by cell counting and 3H-thymidine incorporation, whereas an important decrease in MTT redn. was obsd. Noteworthy, with the highest cholesterol concn. no change in cellular morphol. occurred, and no modification of mitochondrial activity was found with Rhodamine 123. It is concluded that MTT and 3H-thymidine incorporation are not suitable for the evaluation of a putative toxicity of cholesterol and 25-hydroxycholesterol, resp. Therefore, cell counting seems the most accurate method to det. the effects of oxysterols and of cholesterol and endothelial cell growth. The results are discussed in relation to the antiangiogenic activity of the oxysterols.

IT **566-28-9**, 7-Ketocholesterol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(evaluation of cytotoxic effects of oxysterols and of cholesterol on vascular endothelial cell growth in relation to methodol. aspects)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

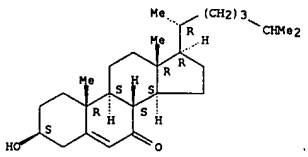


L13 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:430012 CAPLUS
DOCUMENT NUMBER: 127:117125
TITLE: Isolation and structure identification of two constituents with antitumor activity from human fetal liver
AUTHOR(S): Zhang, Qinglin; Wu, Zhuze; Cao, Jurong; Feng, Rui; Du, Zehan
CORPORATE SOURCE: Inst. Radiation Med., Acad. Military Med. Sci., Beijing, 100850, Peop. Rep. China
SOURCE: Junshi Yixue Kexueyuan Yuankan (1996), 20(4), 266-268
CODEN: JYKYEL; ISSN: 1000-5501
PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB 2 Suppressors were sepd. and purified from methanol-acetone ext. of human fetal liver, with the isolation process guarded by suppression of HL-60 cells growth in vitro. The procedure for purifn. included C18 reversed-phase medium pressure chromatog., gel filtration on Sephadex LH-20, and HPLC. The suppressors were identified to be 7-ketocholesterol and 7.beta.-hydroxycholesterol by high resoln. MS and NMR, and both had more evident inhibitory effect on HL-60 cell proliferation than that of the hGM-CFU.

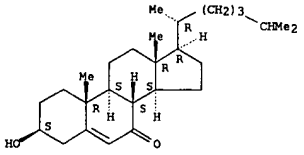
IT **566-28-9P**, 7-Ketocholesterol
RL: PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(isolation and structure identification of two constituents with antitumor activity from human fetal liver)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



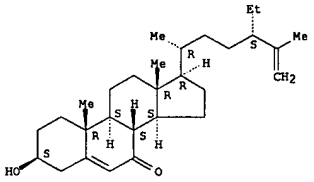
L13 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:250235 CAPLUS
DOCUMENT NUMBER: 124:332980
TITLE: Inhibitory effects of sterols isolated from Chlorella vulgaris on 12-O-tetradecanoylphorbol-13-acetate-induced inflammation and tumor promotion in mouse skin
AUTHOR(S): Yasukawa, Ken; Akihisa, Toshihiro; Kanno, Hiroshi; Kaminaga, Tomohiro; Izumida, Mitsuru; Sakoh, Takashi; Tamura, Toshitake; Takido, Michio
CORPORATE SOURCE: College of Pharmacy, Nihon University, Chiba, 274, Japan
SOURCE: Biol. Pharm. Bull. (1996), 19(4), 573-6
CODEN: BPBLEO; ISSN: 0918-6158
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Inhibitory activity against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice was obsd. in the methanol ext. of Chlorella vulgaris, a green alga. The hexane sol. fraction obtained from the methanol ext. exhibited marked inhibitory activity from which were isolated two .DELTA.5,7-sterols (ergosterol and 7-dehydroporiferasterol), two .DELTA.5,7,9(11)-sterols [9(11)-dehydroergosterol and 7,9(11)-bisdehydroporiferasterol], two 5.alpha.,8.alpha.-epidoxy-.DELTA.6-sterols (ergosterol peroxide and 7-dehydroporiferasterol peroxide), and a 7-oxo-.DELTA.5-sterol (7-oxocholesterol), among others. The .DELTA.5,7-sterols, 5.alpha.,8.alpha.-epidioxy-.DELTA.6-sterols and 7-oxo-.DELTA.5-sterol inhibited TPA-induced inflammation in mice. The 50% ID of these compds. for TPA-induced inflammation was 0.2-0.7 mg/ear. Furthermore, ergosterol peroxide markedly inhibited the tumor-promoting effect of TPA in 7,12-dimethylbenz[a]anthracene-initiated mice.
IT **566-28-9**, 7-Oxocholesterol
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitory effects of Chlorella vulgaris sterols on 12-O-tetradecanoylphorbol-13-acetate-induced inflammation and tumor promotion in mouse skin)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



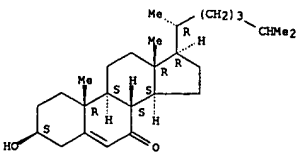
L13 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:1004432 CAPLUS
DOCUMENT NUMBER: 124:170093
TITLE: Oxygenated clerosterols isolated from the marine alga Codium arabicum
AUTHOR(S): Sheu, Jyh-Horng; Liaw, Chin-Chuang; Duh, Chang-Yih
CORPORATE SOURCE: Dep. Marine Resources, Natl. Sun Yat-Sen Univ., Kaohsiung, 804, Taiwan
SOURCE: Journal of Natural Products (1995), 58(10), 1521-6
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Society of Pharmacognosy
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Clerosterol, (24S)-24-ethyl-3-oxocholesta-4,25-dien-6.beta.-ol (I), (24S)-24-ethyl-5.alpha.-hydroperoxycholesta-6,25-dien-3.beta.-ol (II), (24S)-24-ethyl-7-oxocholesta-5,25-dien-3.beta.-ol (III), (24S)-24-ethyl-7.alpha.-hydroperoxycholesta-5,25-dien-3.beta.-ol (IV), and (24S)-24-ethylcholesta-5,25-dien-3.beta.,7.alpha.-diol (V), were isolated from the marine green alga Codium arabicum. A portion of steroid IV was epimerized to (24S)-24-ethyl-7.beta.-hydroperoxycholesta-5,25-dien-3.beta.-ol (VI). LiAlH4 redn. of an inseparable mixt. of IV and VI yielded diol V and (24S)-24-ethylcholesta-5,25-dien-3.beta.,7.beta.-diol (VII). Among these compds., sterols I, II, and IV were isolated for the 1st time from a natural source. Metabolites I-V showed significant cytotoxicity toward various cancer cell lines.
IT **173831-67-9P**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(oxygenated clerosterols isolated from Codium arabicum)
RN 173831-67-9 CAPLUS
CN Stigmasta-5,25-dien-7-one, 3-hydroxy-, (3.beta.,24S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:888257 CAPLUS
DOCUMENT NUMBER: 123:275418
TITLE: Lymphoma cells selected for resistance against the cytotoxic effect of oxygenated sterols are also resistant to nonsteroidal antiestrogens
AUTHOR(S): Low, Yoke L.; Hwang, Peter L. H.
CORPORATE SOURCE: Department of Physiology National University of Singapore, 10 Kent Ridge Crescent, Singapore, 0511, Singapore
SOURCE: Biochim. Biophys. Acta (1995), 1269(1), 32-40
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Oxygenated derivs. of cholesterol and related compds. (oxysterols) have long been known to be cytotoxic to many different cell types. The mechanism of this cytotoxic effect is not fully understood. The lab. has earlier reported that oxysterol cytotoxicity resembles that of nonsteroidal antiestrogens in some aspects: (i) the cytotoxic action of both types of compds. is blocked by inhibitors of protein or RNA synthesis, and (ii) both classes of compds. bind with high affinity to the microsomal antiestrogen binding site, a protein which may mediate the cytotoxicity of its ligands. The authors have now extended these studies by developing cell lines which are resistant to the cytotoxic action of oxysterols. Oxysterol-resistant cells were isolated by exposing 2 murine lymphoma cell lines, K36 and EL4, to incremental concns. of 7-ketocholestanol. Intriguingly, the resistant cells thus obtained also exhibited considerable resistance to the cytotoxic effects of nonsteroidal antiestrogens such as tamoxifen and clomiphene, having LD50 values which were 10-100-fold higher than that of the parental cells. The resistance appeared to be selective for oxysterols and antiestrogens and did not extend to non-specific toxic agents such as azide, ethanol, Triton X-100, or heat. The biochem. basis of the resistance is not clear but is not due to diminished cellular uptake or increased metab. of the cytotoxic agents or to changes in the antiestrogen-binding protein. The availability of the resistant cell lines should facilitate further studies on the mechanism of oxysterol- and antiestrogen-induced cell death.
IT **566-28-9**, 7-Ketocholesterol
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lymphoma cells selected for resistance against cytotoxic effect of oxygenated sterols are also resistant to nonsteroidal antiestrogens)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

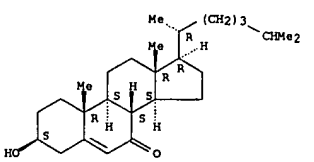


L13 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:503245 CAPLUS
DOCUMENT NUMBER: 122:230779
TITLE: Use of sterols as anti-inflammatory agents
INVENTOR(S): Beneytout, Jean Louis; Andrianarison, Rivo Hery; Chambon, Serge
PATENT ASSIGNEE(S): Biodev, Fr.
SOURCE: Fr. Demande, 8 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2705030	A1	19941118	FR 1993-5665	19930511

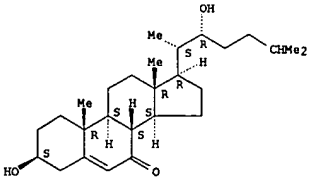
AB Sterols such as cholesterol (I) or cholestane derivs. or precursors are useful as anti-inflammatory agents. A soln. contg. 100 .mu.M I acetate inhibited the activity of 12.mu.g lipoxygenase by 41%. Various pharmaceutical dosage forms are claimed.
IT **566-28-9**, 7-Oxo-cholesterol
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of sterols as anti-inflammatory agents)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



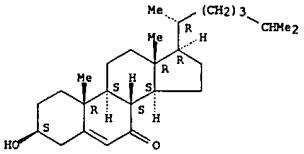
L13 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:485816 CAPLUS
DOCUMENT NUMBER: 109:85816
TITLE: The 22- and 7,22-oxygenated cholesterols. Neoplastic growth inhibition and synergistic effect
AUTHOR(S): Stabursvik, Arnulv
CORPORATE SOURCE: Dep. Chem., Agric. Univ. Norway, As-Nlh, N-1432, Norway
SOURCE: Inst. Natl. Sante Rech. Med., [Colloq.] (1988), 166(Act. Biol. Oxysterols), 289-93
CODEN: CINMDE; ISSN: 0768-3154
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment of rats bearing dimethylbenzanthracene-induced mammary carcinomas with 7.beta.,22R-dihydroxycholesterol inhibited tumor growth and increased the life span. The in vitro effect of the 7-keto deriv. was comparable to that of the 7.beta.-OH compd., whereas the 7.alpha.-OH compd. was ineffective. Addn. of small amts. of 22R-hydroxycholesterol, which had no effect alone, doubled the antitumor effect of the 7.beta.-OH compd.
IT **104786-67-6**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neoplasm inhibition by, in mammary carcinoma)
RN 104786-67-6 CAPLUS
CN Cholest-5-en-7-one, 3,22-dihydroxy-, (3.beta.,22R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



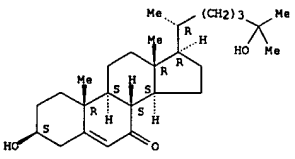
L13 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:560958 CAPLUS
DOCUMENT NUMBER: 93:160958
TITLE: Hypocholesterolemic activity of phytosterol. II
AUTHOR(S): Tabata, Toshikazu; Tanaka, Mitsuo; Iio, Toshihiro
CORPORATE SOURCE: Showa Coll. Pharm. Sci., Tokyo, Japan
SOURCE: Yakugaku Zasshi (1980), 100(5), 546-52
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The hypocholesterolemic activities of phytosterols and related compds. were compared in rats receiving a 3% cholesterol [57-88-5]- contg. diet. The rats were i.v. injected for 5 days with emulsions of saline-albumin contg. each sterol. The greatest effect on lowering liver cholesterol, triglyceride, and fatty acid levels was shown by stigmasterol (I) [83-48-7], followed by .beta.-sitosterol [83-46-5], stigmastanol [83-45-4], ergosterol [57-87-4] and 7-ketocholesterol [566-28-9]. On the other hand, I palmitate [2308-84-1] and I stearate [23838-16-6] showed considerably lower activity than I. No effect could be seen in I acetate [4651-48-3], which is not found in nature. After injections, I in liver was present mainly in a free form and the palmitate or the stearate changed partly to the free form, 20% or 25% of the injected amt., resp. However, I acetate remained unchanged after injection. The cytochrome P-450 [9035-51-2] content of hepatic microsome from hypercholesterolemic rats was decreased by treatment with I and similar findings were obtained in microsomes from livers of normal or phenobarbital-treated rats which had been given I. The presence of a free hydroxy group at the C-3 position in phytosterols is apparently necessary for the hypocholesterolemic activities and a double bond at the C-5 position and a side-chain at the C-17 position, may also relate to these activities.
IT **566-28-9**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticholesteremic activity of, structure in relation to)
RN 566-28-9 CAPLUS
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:198 CAPLUS
DOCUMENT NUMBER: 88:198
TITLE: Chemistry and biochemistry of Chinese drugs. Part II. Hydroxylated sterols, cytotoxic towards cancerous cells: synthesis and testing
AUTHOR(S): Nagano, Hajime; Poyser, J. Philip; Cheng, Kwok-Ping; Luu Bang; Ourisson, Guy; Beck, Jean Paul
CORPORATE SOURCE: Inst. Chim., Univ. Louis Pasteur, Strasbourg, Fr.
SOURCE: J. Chem. Res. (S) (1977), (9), 218
CODEN: JRPSDC
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The cytotoxic activity was detd. of 23 cholesterol derivs. hydroxylated at C-1, -6, -7, -22, or -25, 20 cholesterol derivs. unsatd. in the side chain and hydroxylated at C-7, -20, -22, -23, or -24, 10 steroids hydroxylated at C-3 and carrying another O function, with varying side chain, and 5 tetracyclic triterpenes, esp. inotodiol derivs. The activity was measured against HTC and ZHC hepatoma cells and normal fibroblast 3T3 cells. Desmosterol derivs. were the most active and most selective. New compds. were prepd. by std. methods. In contrast to the report by A. N. Shivrina (1966), inotodiol is inactive.
IT **64907-23-9P 64907-26-2P 64933-64-8P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and cytotoxicity of)
RN 64907-23-9 CAPLUS
CN Cholest-5-en-7-one, 3,25-dihydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

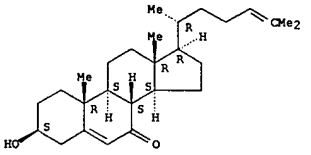
Absolute stereochemistry.



RN 64907-26-2 CAPLUS
CN Cholesta-5,24-dien-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

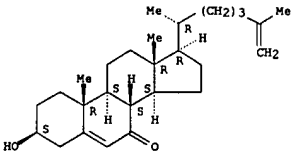
Absolute stereochemistry.

L13 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 64933-64-8 CAPLUS
CN Cholesta-5,25-dien-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib ab hitstr 1-14

L14 ANSWER 1 OF 14 USPATFULL
ACCESSION NUMBER: 2002:133975 USPATFULL
TITLE: Stereoselective synthesis of 24-hydroxylated compounds useful for the preparation of aminosterols, vitamin D analogs, and other compounds
INVENTOR(S): Kinney, William A., Richboro, PA, UNITED STATES
Jones, Steven, West Chester, PA, UNITED STATES
Zhang, Xuehai, E. Norriton, PA, UNITED STATES
Rao, Meena N., Lansdale, PA, UNITED STATES
Bulliard, Michel, Angers, FRANCE
Meckler, Harold, Delmar, NY, UNITED STATES
Lee, Nancy, Foxboro, MA, UNITED STATES
PATENT ASSIGNEE(S): Magainin Pharmaceuticals, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002068834	A1	20020606
APPLICATION INFO.:	US 2001-833055	A1	20010412 (9)

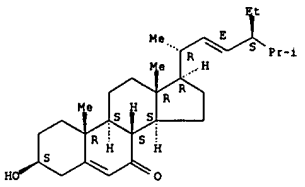
RELATED APPLN. INFO.: Division of Ser. No. US 1997-985576, filed on 5 Dec 1997, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-32378P	19961206 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MORGAN, LEWIS & BOCKIUS, 1800 M STREET NW, WASHINGTON, DC, 20036-5869
NUMBER OF CLAIMS: 52
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 19 Drawing Page(s)
LINE COUNT: 2270
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is described for stereoselectively reducing an unsaturated alkyl ketone substituent attached to a fused ring base. In this method, the unsaturated alkyl ketone reacts with a chiral oxazaborolidine reagent. This reaction stereoselectively reduces the unsaturated alkyl ketone to an unsaturated alkyl alcohol. The unsaturated alkyl alcohol can be further reduced, if desired, to produce a saturated alkyl alcohol. The fused ring base can be, for example, a steroid ring base or a base of a vitamin D analog. The process in accordance with the invention can be used with an alkeneone substituent (e.g., a 22-ene-24-one substituent) or an alkyneone substituent (e.g., a 22-yne-24-one substituent) on a steroid ring base to make squalamine or other useful aminosterol compounds and intermediates for making aminosterol compounds.
IT **36449-99-7P**, 7-Oxostigmasterol
(synthesis of 24-hydroxylated compds. via stereoselective redn., and their use in prepn. of aminosterols)
RN 36449-99-7 USPATFULL
CN Stigmasta-5,22-dien-7-one, 3-hydroxy-, (3.beta.,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 1 OF 14 USPATFULL (Continued)

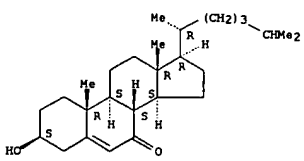


L14 ANSWER 2 OF 14 USPATFULL
ACCESSION NUMBER: 2001:131458 USPATFULL
TITLE: Process for allylic oxidation using metal hypochlorite and alkyl hydroperoxide
INVENTOR(S): Marwah, Padma, 6710 Spring Grove Ct., Middleton, WI, United States 53562
Lardy, Henry A., 1829 Thorstrand Rd., Madison, WI, United States 53705
Marwah, Ashok Kumar, 6710 Spring Grove Ct., Middleton, WI, United States 53562

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6274746	B1	20010814
APPLICATION INFO.:	US 2000-651604		20000830 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Badio, Barbara P.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 1007
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to a process for effecting the allylic oxidation of an allylic compound having at least two allylic hydrogen atoms on the same carbon atom into corresponding .alpha.,.beta.-unsaturated carbonyl compound, using a combination of a metal hypochlorite and an alkyl hydroperoxide in a mixture of suitable conventional organic solvent(s) and/or water at a temperature of between about -5.degree. C. to +25.degree. C.
IT **566-28-9P**
(process for allylic oxidn. using metal hypochlorite and alkyl hydroperoxide)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 3 OF 14 USPATFULL
ACCESSION NUMBER: 2001:112547 USPATFULL
TITLE: Stereoselective synthesis of 24-hydroxylated compounds useful for the preparation of aminosterols, vitamin D analogs, and other compounds
INVENTOR(S): Kinney, William A., Richboro, PA, United States
Jones, Steven, West Chester, PA, United States
Zhang, Xuehai, E. Norriton, PA, United States
Rao, Meena N., Lansdale, PA, United States
Bulliard, Michel, Angers, France
Meckler, Harold, Delmar, NY, United States
Lee, Nancy, Foxboro, MA, United States
PATENT ASSIGNEE(S): Magainin Pharmaceuticals Inc., Plymouth Meeting, PA, United States (U.S. corporation)

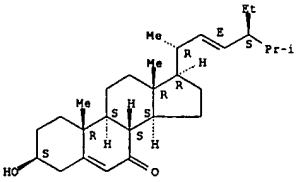
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6262283	B1	20010717
APPLICATION INFO.:	US 1997-985876		19971205 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-32378P	19961206 (60)
	US 1997-17627P	19970516 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Clardy, S. Mark
ASSISTANT EXAMINER: Pryor, Alton
LEGAL REPRESENTATIVE: Morgan, Lewis & Bockius LLP
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 29 Drawing Figure(s); 19 Drawing Page(s)
LINE COUNT: 2206
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is described for stereoselectively reducing an unsaturated alkyl ketone substituent attached to a fused ring base. In this method, the unsaturated alkyl ketone reacts with a chiral oxazaborolidine reagent. This reaction stereoselectively reduces the unsaturated alkyl ketone to an unsaturated alkyl alcohol. The unsaturated alkyl alcohol can be further reduced, if desired, to produce a saturated alkyl alcohol. The fused ring base can be, for example, a steroid ring base or a base of a vitamin D analog. The process in accordance with the invention can be used with an alkeneone substituent (e.g., a 22-ene-24-one substituent) or an alkyneone substituent (e.g., a 22-yne-24-one substituent) on a steroid ring base to make squalamine or other useful aminosterol compounds and intermediates for making aminosterol compounds.
IT **36449-99-7P**, 7-Oxostigmasterol
(synthesis of 24-hydroxylated compds. via stereoselective redn., and their use in prepn. of aminosterols)
RN 36449-99-7 USPATFULL
CN Stigmasta-5,22-dien-7-one, 3-hydroxy-, (3.beta.,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 3 OF 14 USPATFULL (Continued)



L14 ANSWER 4 OF 14 USPATFULL

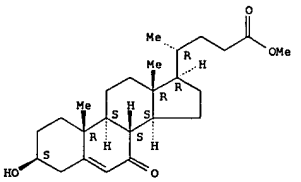
ACCESSION NUMBER: 1998:150955 USPATFULL
TITLE: 7-substituted 4-aza cholanic acid derivatives and their use
INVENTOR(S): Graham, Donald W., Mountainside, NJ, United States
Carlin, Josephine R., Annandale, NJ, United States
Tolman, Richard L., Warren, NJ, United States
Chiu, Shuet-Hing Lee, Westfield, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5843953		19981201	
	WO 9612705		19960502	
APPLICATION INFO.:	US 1997-809506		19970324	(8)
	WO 1995-US13112		19951020	
			19970324	PCT 371 date
			19970324	PCT 102(e) date

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-328622, filed on 25 Oct 1994, now patented, Pat. No. US 5595996
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rotman, Alan L.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Winokur, Melvin
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 597
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (I) wherein: the dotted line indicates that a double bond may be present or absent; R.sup.1 is H, methyl or ethyl; R.sup.2 is .alpha.- or .beta.-C.sub.1-10 straight or branched alkyl; R.sup.3 is CO.sub.2 H, CN, CO.sub.2 R.sup.4, CONHR.sup.4, or CON(R.sup.4).sub.2 ; R.sup.4 is H, C.sub.1-10 straight or branched alky, aryl, heteroaryl, or aralkyl; Aryl is phenyl, substituted phenyl, naphthyl, or biphenyl; Heteroaryl is pyridil, pyrrolyl, thienyl, furanyl or quinolinyl; and Aralkyl is C.sub.1-10 alkyl substituted with one to three phenyl or substituted phenyl moieties; and their pharmaceutically acceptable salts are described. These compounds are 5.alpha.-reductase type 1 inhibitors. They may be used for treating conditions associated with an excess of DHT, either alone or in combination with other 5.alpha.-reductase inhibitors. ##STR1##
IT **31427-15-3P**
(synthesis of 4-aza cholanic acid derivs. for use in treatment of conditions assocd. with excess dihydrotestosterone)
RN 31427-15-3 USPATFULL
CN Chol-5-en-24-oic acid, 3-hydroxy-7-oxo-, methyl ester, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 4 OF 14 USPATFULL (Continued)



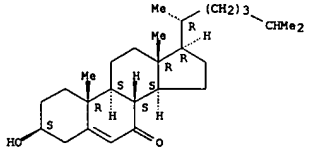
L14 ANSWER 5 OF 14 USPATFULL

ACCESSION NUMBER: 1998:147467 USPATFULL
TITLE: Reduction of hair growth
INVENTOR(S): Henry, James P., 10257 Meadow Fence Ct., Myersville, MD, United States 21773
Ahluwalia, Gurpreet S., 8632 Stableview Ct., Gaithersburg, MD, United States 20882
Shander, Douglas, 16112 Howard Landing Dr., Gaithersburg, MD, United States 20878

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5840752		19981124	
APPLICATION INFO.:	US 1996-754556		19961121	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: MacMillan, Keith D.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
LINE COUNT: 328
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mammalian hair growth is reduced by applying to the skin an inhibitor of a cholesterol synthetic pathway enzyme.
IT **566-28-9**, 7-Ketocholesterol
(skin application of inhibitors of cholesterol synthetic pathway enzymes for redn. of unwanted hair growth)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



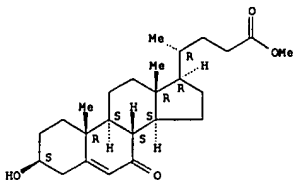
L14 ANSWER 6 OF 14 USPATFULL
ACCESSION NUMBER: 97:5975 USPATFULL
TITLE: 7-substituted 4-aza cholanic acid derivatives and their use
INVENTOR(S): Graham, Donald W., Mountainside, NJ, United States
Carlin, Josephine R., New Brunswick, NJ, United States
Chiu, Shuet-Hing L., Westfield, NJ, United States
Tolman, Richard L., Warren, NJ, United States
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5595996		19970121	
APPLICATION INFO.:	US 1994-328622		19941025	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rotman, Alan L.
LEGAL REPRESENTATIVE: Fitch, Catherine D., Giesser, Joanne M., Winokur, Melvin
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 607
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the Formula I ##STR1## wherein: the dotted line indicates that a double bond may be present or absent; R.sup.1 is H, methyl or ethyl; R.sup.2 is .alpha.- or .beta.-C.sub.1-10 straight or branched alkyl; R.sup.3 is CO.sub.2 H, CN, CO.sub.2 R.sup.4, COHNR.sup.4, or CON(R.sup.4).sub.2 ; R.sup.4 is H, C.sub.1-10 straight or branched alkyl, aryl, heteroaryl, or aralkyl; Aryl is phenyl, substituted phenyl, naphthyl, or biphenyl; Heteroaryl is pyridyl, pyrrolyl, thienyl, furanyl or quinolinyl; and Aralkyl is C.sub.1-10 alkyl substituted with one to three phenyl or substituted phenyl moieties; and their pharmaceutically acceptable salts are described. These compounds are 5.alpha.-reductase type 1 inhibitors. They may be used for treating conditions associated with an excess of DHT, either alone or in combination with other 5.alpha.-reductase inhibitors.
IT **31427-15-3**
(prepn. of azacholanoic acid derivs. as 5.alpha.-reductase inhibitors)
RN 31427-15-3 USPATFULL
CN Chol-5-en-24-oic acid, 3-hydroxy-7-oxo-, methyl ester, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 6 OF 14 USPATFULL (Continued)

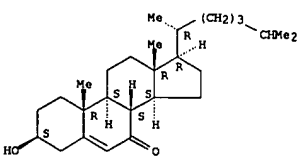


L14 ANSWER 7 OF 14 USPATFULL
ACCESSION NUMBER: 84:20038 USPATFULL
TITLE: Water-soluble cholesterol derivative
INVENTOR(S): Arakawa, Yoshio, 10-18, Ezakacho 1-chome, Suita-shi, Japan
Takanabe, Atsuyuki, 29-19, Nagao-Higashicho 2-chome, Hirakata-shi, Japan
Uemura, Yahiro, 5-18, Mitsuyacho, Hirakata-shi, Japan
Funakoshi, Satoshi, 16-5, Aoyama 1-chome, Katano-shi, Japan
Suyama, Tadakazu, 3-7, Tanabecho, Matsuigaoka 4-chome, Tsuzuki-gun, Kyoto, Japan

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4442037		19840410	
	WO 8203175		19820930	
APPLICATION INFO.:	US 1982-432938		19820928	(6)
	WO 1981-JP56		19810313	
			19820928	PCT 371 date
			19820928	PCT 102(e) date

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 314
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Complexes of albumin combined with organic dibasic acid half esters, such as those of succinic acid and phthalic acid, of 7-hydroxycholesterol are soluble in water and have excellent immunosuppressive and anti-inflammatory action.
IT **566-28-9**
(acylation of, by succinic anhydride)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



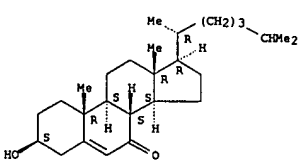
L14 ANSWER 8 OF 14 USPATFULL
ACCESSION NUMBER: 81:66945 USPATFULL
TITLE: Process for the preparation of cholesterol derivatives
INVENTOR(S): Arakawa, Yoshio, Suita, Japan
Takanabe, Atuyuki, Hirakata, Japan
Uemura, Yahiro, Hirakata, Japan
Funakoshi, Satoshi, Katano, Japan
Satoh, Daisuke, Nishinomiya, Japan
PATENT ASSIGNEE(S): The Green Cross Corporation, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4304726		19811208	
APPLICATION INFO.:	US 1980-156091		19800603	(6)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1979-76767	19790620

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 353
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB New organic dibasic acid half esters of 7-ketocholesterol and of 7-hydroxycholesterol represented by the general formula ##STR1## (wherein R.sub.1 is .dbd.O or --OH and R.sub.2 is a C.sub.1 -C.sub.5 alkylene group or a phenylene group) and physiologically acceptable salts thereof. These compounds are effective as an immunosuppressive or an anti-inflammatory agent.
IT **566-28-9**
(esterification of, by succinic anhydride)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

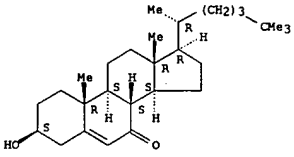


L14 ANSWER 9 OF 14 USPATFULL
ACCESSION NUMBER: 81:61542 USPATFULL
TITLE: 25-Alkylcholest-5-ene-3 .beta.,22-diols and esters thereof
INVENTOR(S): Chorvat, Robert J., Arlington Heights, IL, United States
PATENT ASSIGNEE(S): G. D. Searle & Co., Chicago, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4299774		19811110
APPLICATION INFO.:	US 1980-145110		19800430 (6)

DISCLAIMER DATE: 19970527
RELATED APPLN. INFO.: Continuation of Ser. No. US 1978-929068, filed on 28 Jul 1978, now Defensive Publication No. which is a continuation-in-part of Ser. No. US 1977-828385, filed on 29 Aug 1977, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Serauskas, Joy A., Drehkoff, W. Dennis
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 258
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 25-Alkylcholest-5-ene-3.beta.,22-diols and esters thereof adapted to inhibit the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase are disclosed.
IT **70778-58-4P**
(prepn. and acylation of, by succinic anhydride)
RN 70778-58-4 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

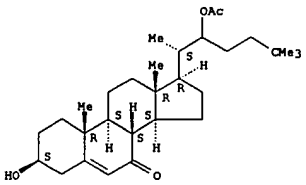
Absolute stereochemistry.



IT **70778-56-2P**
(prepn. of)
RN 70778-56-2 USPATFULL
CN Cholest-5-en-7-one, 22-(acetyloxy)-3-hydroxy-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 9 OF 14 USPATFULL (Continued)

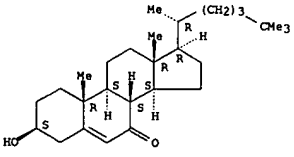


L14 ANSWER 10 OF 14 USPATFULL
ACCESSION NUMBER: 80:13855 USPATFULL
TITLE: 25-Alkyl-3.beta.-hydroxycholest-5-en-7-ones and esters thereof
INVENTOR(S): Chorvat, Robert J., Arlington Heights, IL, United States
PATENT ASSIGNEE(S): G. D. Searle & Co., Skokie, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4193930		19800318
APPLICATION INFO.:	US 1978-928664		19780728 (5)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1977-828385, filed on 29 Aug 1977, now Defensive Publication No.
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Henes, James R., Brown, John M.
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 272
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 25-Alkyl-3.beta.-hydroxycholest-5-en-7-ones and esters thereof adapted to lower serum cholesterol and inhibit the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase are disclosed.
IT **70778-58-4P**
(prepn. and esterification of, with dicarboxylic acid derivs.)
RN 70778-58-4 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-25-methyl-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



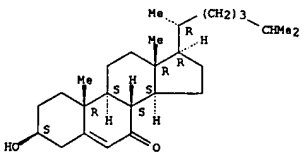
L14 ANSWER 11 OF 14 USPATFULL
ACCESSION NUMBER: 79:27040 USPATFULL
TITLE: Cholesterol derivative-based medicaments acting on bio-protective mechanisms
INVENTOR(S): Kitame, Fumio, Sendai, Japan
Saitoh, Hiroshi, Sendai, Japan
Ishida, Nakao, Sendai, Japan
PATENT ASSIGNEE(S): The Green Cross Corporation, Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4157391		19790605
APPLICATION INFO.:	US 1977-804239		19770607 (5)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1977-18939	19770223

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 288
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 7-Hydroxycholesterol and 7-ketocholesterol can be used as a medicament having a pharmacodynamic action on the bio-protective mechanisms, and thus they are useful as an immunoregulatory agent or antiphlogistic agent.
IT **566-28-9P**
(prepn. of, as antiinflammatory and immunosuppressant)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

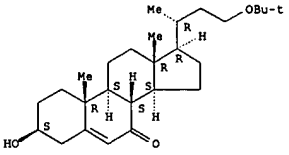


L14 ANSWER 12 OF 14 USPATFULL
ACCESSION NUMBER: 78:63710 USPATFULL
TITLE: 20/22/23/24-Oxa-7-oxocholesterols and esters thereof
INVENTOR(S): Dygos, John H., Northbrook, IL, United States
PATENT ASSIGNEE(S): G. D. Searle, Chicago, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4125544		19781114
APPLICATION INFO.:	US 1977-804951		19770609 (5)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Brown, John M.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 682
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Preparation and the antimicrobial and antihypercholesterolemic utility of 20/22/23/24-oxa-7-oxocholesterols and esters thereof are disclosed.
IT **69436-63-1P**
(prepn. and acylation of)
RN 69436-63-1 USPATFULL
CN 24-Norchol-5-en-7-one, 23-(1,1-dimethylethoxy)-3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

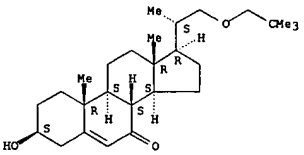
Absolute stereochemistry.



IT **69436-44-8P 69436-48-2P 69436-52-8P 69436-56-2P 69436-60-8P**
(prepn. of)
RN 69436-44-8 USPATFULL
CN Pregn-5-en-7-one, 3-hydroxy-20-(3-methylbutoxy)-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

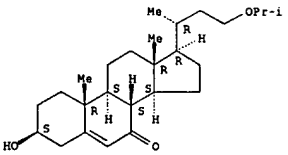
Absolute stereochemistry.

L14 ANSWER 12 OF 14 USPATFULL (Continued)
Absolute stereochemistry.

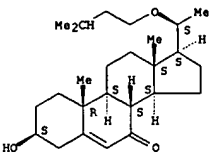


RN 69436-60-8 USPATFULL
CN 24-Norchol-5-en-7-one, 3-hydroxy-23-(1-methylethoxy)-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

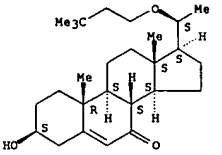


L14 ANSWER 12 OF 14 USPATFULL (Continued)



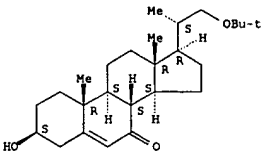
RN 69436-48-2 USPATFULL
CN Pregn-5-en-7-one, 20-(3,3-dimethylbutoxy)-3-hydroxy-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 69436-52-8 USPATFULL
CN Pregn-5-en-7-one, 21-(1,1-dimethylethoxy)-3-hydroxy-20-methyl-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



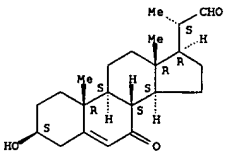
RN 69436-56-2 USPATFULL
CN Pregn-5-en-7-one, 21-(2,2-dimethylpropoxy)-3-hydroxy-20-methyl-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

L14 ANSWER 13 OF 14 USPATFULL
ACCESSION NUMBER: 78:54534 USPATFULL
TITLE: Novel method for preparing cholesta-5,7-diene 3.beta.,25-diol and derivatives thereof
INVENTOR(S): Salmond, William G., Kalamazoo, MI, United States
PATENT ASSIGNEE(S): The Upjohn Company, Kalamazoo, MI, United States (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4116985		19780926
APPLICATION INFO.:	US 1976-708023		19760726 (5)

DISCLAIMER DATE: 19931130
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Roberts, Elbert L.
LEGAL REPRESENTATIVE: Barancik, Martin B.
NUMBER OF CLAIMS: 90
EXEMPLARY CLAIM: 1
LINE COUNT: 616
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A new method for synthesizing cholesta-5,7-diene-3.beta.,-25-diol and cholesta-5,7-diene-1.alpha.,3.beta.,25-triol has been discovered. ##STR1## wherein R is hydrogen or hydroxy. Various intermediates and reaction steps are claimed.
IT **22287-19-0**
(reaction of, with isobutylene oxide and methyltriphenylphosphonium bromide)
RN 22287-19-0 USPATFULL
CN Pregn-5-ene-20-carboxaldehyde, 3-hydroxy-7-oxo-, (3.beta.,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 14 OF 14 USPATFULL
ACCESSION NUMBER: 77:23980 USPATFULL
TITLE: Methods and compounds for producing specific antibodies
INVENTOR(S): Gross, Stanley J., Encino, CA, United States
PATENT ASSIGNEE(S): Biological Developments, Inc., Encino, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4022878		19770510
APPLICATION INFO.:	US 1974-528044		19741129 (5)

RELATED APPLN. INFO.: Division of Ser. No. US 1972-253632, filed on 15 May 1972, now abandoned which is a continuation-in-part of Ser. No. US 1970-45558, filed on 11 Jun 1970, now abandoned And Ser. No. US 1970-89929, filed on 16 Nov 1970, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Padgett, Benjamin R.
ASSISTANT EXAMINER: Nucker, Christine M.
LEGAL REPRESENTATIVE: McAulay, Fields, Fisher & Goldstein
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 774
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to a novel method of producing purified antibodies which are truly specific for native homologous hapten or antigen by administering artificial antigens as described therein to an antibody producing host followed by isolation and purification.

IT **566-28-9**
(reaction of, with carboxyphenylhydrazine, antibody prodn. in relation to)
RN 566-28-9 USPATFULL
CN Cholest-5-en-7-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.